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Brain

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A Journal of Neurology

EDITED BY

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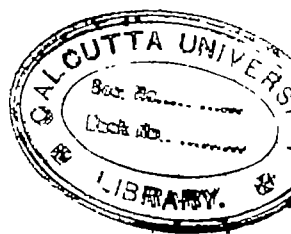
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PART I., VOL. 34.

Original Articles and Clinical Cases.

THE SENSE OF PRESSURE IN THE FACE, EYE, AND TONGUE.

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I. INTRODUCTION.

Despite the large amount of work that has been devoted to the investigation of the sensory innervation of the face and the afferent functions of the trigeminal nerve there are still some points that need elucidation. One of these is the condition of sensibility to pressure, and to pain produced by pressure, on the deeper structures, especially after complete division of the root of the fifth nerve, or removal of the Gasserian ganglion.

Cushing [1] makes no specific mention of the investigation of pressure-sense in his cases, but he states that the more anterior of the lines that delimit the area of the trigeminal anæsthesia posteriorly

"bounds the area within which anæsthesia is complete to all forms of sensation." This area includes the greater part of the fifth distribution.

Morrison Davies [2] found that "deep pressure is occasionally appreciated" in parts over which light touch and pressure-touch are absent. This was especially so when the soft tissues were strongly compressed on the underlying bone. But he mentions cases in which teeth were extracted, another in which an eye was excised, and two others in which extensive operations were performed on the affected side of the face without producing pain, though no anæsthetic was employed.

Ivy and Johnson [3], however, observed two cases, and refer to another under Spiller's care, in which there was apparently complete destruction of the trigeminal root or of its ganglion, yet pressure could be appreciated over the area of cutaneous anæsthesia. They drew the conclusion that the facial nerve "conveys fibres of deep or pressure-sensibility from the muscles which it supplies with motor fibres."

On the other hand Mills [4], who has recently dealt with the subject exhaustively, found the sense of pressure lost in the areas over which there was cutaneous anæsthesia and states the conclusion that "the sense of pressure is represented in the fifth and not in the seventh nerve."

The existence of such divergent statements justifies the re-investigation of the question on suitable cases.

When pressure is applied to the face the amount of muscular effort called forth to resist the tendency of the head to move, doubtless affords a measure of the pressure applied. There is also, however, a purely nervous mechanism by which pressure can be appreciated even when wholly inadequate to produce movement. This mechanism enables us not only to perceive and to estimate, but also to localize pressure; and it has in addition a protective function, for, with the feeling of increasing pressure, discomfort arises and grows quickly into pain. This pressure-sense is distinct from the sense by which we perceive mere contact, such as the touch of cotton-wool; and it may exist unimpaired, as Head and Rivers have shown, even in the complete absence of cutaneous sensibility. The path of these pressure sense-impulses from the face has not yet been finally determined. By examining well-defined lesions of the fifth, seventh, and twelfth nerves we have endeavoured to gain some further information on the following points:—

- (1) The relation of the deep afferents of the face, eye, and tongue to—
 - (a) The roots of the fifth nerve.
 - (b) The Gasserian ganglion.
 - (c) The origin of the fifth nerve.

(2) The relation of the pressure-touch and pain-fibres of the face to the seventh nerve—

- (a) After its exit from the stylo-mastoid foramen.
- (b) Between the Fallopian aqueduct and the stylo-mastoid foramen.
- (c) In the Fallopian aqueduct.
- (d) From the nucleus to the Fallopian aqueduct.

(3) The relation of the pressure-fibres of the tongue to the twelfth nerve.

Through the kindness of Sir Victor Horsley and the Medical Committee of the National Hospital we were enabled to examine a number of patients in whom intracranial operations had been performed upon the fifth nerve for the relief of neuralgia. Several of these patients proved to be mentally too unstable to give trustworthy results. The others, eleven in number, comprised eight cases of removal of the Gasserian ganglion; in three of these the motor supply to the forehead was cut in the skin incision, and in them we observed the effect of a combined lesion of the fifth and of the peripheral seventh; two cases of section of the second and third roots, and one of section of the second root only. We also examined ten cases of complete seventh nerve palsy, from lesions at various levels, arising from several causes; in two the paralysed seventh nerve was subsequently cut after its exit from the stylo-mastoid foramen and the peripheral portion sutured to the central end of a completely divided twelfth. Our cases of central lesions were unsatisfactory; in one an extra-cerebellar tumour had been removed many years before, and among the sequelæ was a unilateral complete fifth and seventh palsy, but the patient was somewhat demented; the other was a case of extra-cerebellar tumour in which the paralysis of the fifth and seventh was incomplete.

The investigations were made under conditions which ensured to the patient as much freedom from suggestion and distraction as possible.

II. TACTILE PRESSURE.

So long as cutaneous sensibility to light touch is intact it is impossible to attempt accurately to investigate tactile pressure. We hoped by cocainization to get rid of the cutaneous sensibility, and therefore ionized upon the face a 10 per cent. solution of cocaine for ten to twenty minutes by means of a current of 10 to 20 ma., and tested ourselves and patients. But it proved impossible to anæsthetize the face to

the light touch stimulus of a von Frey's No. 4 hair [21 gm./mm.²] without diminishing the sensibility to pressure-touch. We were therefore compelled to fall back upon those cases where the skin had been rendered insensitive by removal of the Gasserian ganglion or division of the branches of the fifth nerve.

In each of the fifth nerve cases the area of cutaneous anæsthesia was first outlined. The region insensitive to light touch was determined by means of von Frey's tactile hairs. The application of even a No. 4 hair produced perceptible dimpling of the skin, so each tactile impulse was to a minute extent diffused. The boundary line obtained by marking out the anæsthetic area by proceeding from sensitive toward insensitive regions rarely quite coincided with that obtained when testing in the reverse direction. In proceeding from the sensitive to the insensitive area the patient's attention was awakened and he appreciated stimuli of less intensity than would have been otherwise the case; the anæsthetic zone was thus far smaller than when testing proceeded in the reverse direction, and was encircled by a narrow band or soft border of partial loss. This soft border was best seen in front of and at right angles to the ear; thence it gradually tapered off upon the cheek. A No. 4 hair, the equivalent of a pressure of 21 gm./mm.², was found invariably to be above the tactile threshold on every region of the normal face, so it was always used to map out the area anæsthetic to light touch, within which to test the appreciation of pressure-touch.

To investigate pressure-touch we used a convenient little æsthesiometer devised by Dr. Gordon Holmes. It consists of a thin steel rod surrounded by a metal or vulcanite case, within which it moves in the direction only of its length; each end projects about an inch beyond the enclosing tube; that which applies pressure to the skin is protected by a cork pad; the other, which is a support for weights, is encircled at its exit from the case by a small metal shelf. The extent of the contact-surface of the cork pad is 1 square decimetre, and the æsthesiometer, weighing 2 gm., thus exerts a pressure of 2 gm./dm.²; but by means of disc-shaped weights, pierced in the centre so that they may be threaded on the rod till they rest on the supporting shelf, a graduated increase of pressure can be obtained.

The application of the instrument alone, a pressure of 2 gm./dm.², was readily appreciated as pressure everywhere on the normal half of the face; on the affected side, within the outline of the light touch anæsthesia, was invariably an area of complete insensibility to this

pressure. The extent of the separation of the boundaries of these two anæsthetic areas varied from 0.5 to 1.0 cm. on the cheek, but was often imperceptible over the forehead. With a pressure of 10 gm./dm.² the border lay wholly within the area mapped out by 2 gm./dm.² (fig. 1); and with 20 gm./dm.² the pressure-touch anæsthesia continued to retreat till the new border was separated on the cheek by an interval of 1.0 to 1.5 cm. from the first. Within the innermost border there was



FIG. 1.

Case 12.—Section of the second and third roots of the fifth nerve. The outermost line indicates the limit of light touch anæsthesia; the middle, of 10 gm./dm.; and the innermost of 65 gm./dm. pressure. The crosses mark a soft border of inconstant extent.

total anæsthesia to 20 gm./dm.²; without, was an area insensitive to 10 gm./dm.², and beyond this, encased in a zone anæsthetic to light touch, was an area insensitive to 2 gm./dm.²

The area of anæsthesia to 65 gm./dm.², the maximum pressure of the æsthesiometer, varied; usually it was a counterpart on a smaller scale of that mapped out with 20 gm./dm.²; but around the angle of the mouth, over the side of the nose, on the malar bone, and less frequently on the forehead, sensitive islets now sometimes appeared inside the

anæsthetic zone; and occasionally the border of the pressure anæsthesia, instead of running roughly parallel to the limiting line of the anæsthesia to light touch, curved convexly downwards and forwards from the hair-line, about 3 cm. in front of the ear, across the cheek, to the inner canthus (fig. 2).

After extirpation of the Gasserian ganglion, or section of the second and third roots, and even of the second root alone, there was total loss of perception of 65 gm./dm.² pressure on the conjunctiva.



FIG. 2.

Case 17.—Extirpation of Gasserian ganglion. To show area of anæsthesia to light touch, continuous line, and to 65 gm./dm.² pressure, dotted line.

To the same pressure a more or less severe degree of anæsthesia was always present over the affected half of the anterior part of the supported protruded tongue; in the case of the section of only the second root the tongue recovered apparently normal sensibility in the course of a week. Accurately to define the extent of the loss on the tongue was impossible owing to the structure and mobility of the organ.

The loss of sensibility to pressure-touch was greatest within forty-eight hours of the operation. Indeed, in two cases, for nearly a week it

appeared to be absolute. In no case, even after the lapse of several years, was the recovery striking, but in old cases some residual sensibility to pressure-touch could always be demonstrated.

The degree of loss varied in different regions. In the eye, in all cases, the loss was as great as we, having regard for the patient's eye, cared to demonstrate. The loss was identical when the Gasserian ganglion had been removed, when the second and third roots alone had been cut, or even when the second root only was wanting. The pressure-touch sense of the eye may pass by the second root alone, but more probably may be accidentally destroyed by operations upon that root. In the case where the second root alone was cut, a week after operation the tongue appeared to be normal; its pressure-sense was invariably affected in all the other cases, but the degree was very inconstant. Probably its pressure-touch fibres pass by the third root of the fifth nerve.

On the face the area of anæsthesia to pressure-touch appears at first sight to be more restricted than the area of cutaneous anæsthesia. The difference is least obvious over the forehead, most over the cheek, and varies according to the pressure employed. The application of the æsthesiometer produced visible deformation of structure, not only at the site of application, but also over an irregularly circular zone whose centre lay in the contact area. Pressure thus produces two sets of impressions—a deep localized group from the pressure-contact area and a diffuse group rapidly becoming superficial, arising from the tension produced on the surrounding tissues. Both these groups increase in proportion as the pressure increases, but even with a uniform pressure the stimuli from the tension zone obviously increase in proportion with the mobility of the tissues. In testing from insensitive towards sensitive parts while yet the pressure-contact area itself is anæsthetic, a segment of the zone of tissue-tension adequate to elicit a response may encroach upon the normal skin. Hence, the boundary of the pressure-anæsthesia always fell within, and was roughly parallel to, the boundary of the cutaneous anæsthesia. The forehead tissues yield little, the cheek tissues much; hence the disproportion between the apparent shrinkage on the forehead and on the cheek. And, for the same reason, in attempting to define the areas of anæsthesia to different degrees of pressure we outlined a progressively smaller area with every increase of pressure, but in all cases the shape remained essentially that of the cutaneous anæsthesia area. The extent of the divergence between the boundaries for light touch and pressure at any site was thus the index merely of the effective

distance of the diffuse tension created there by the pressure employed. Are the stimuli from the tension zone or from the pressure-contact area the real measure of the sensibility of the area? The two cannot be separated: both are factors of the pressure-sensibility of the area. But unless the effect of the pressure is strictly localized to the area tested, the result affords no criterion of the sensibility of the area. To make the tension zone and the contact area quite identical is impossible, but this is practically attained by the use of light pressures over rigid areas. Our results with 2 gm./dm.² pressure are therefore the best index to the real extent of the pressure-anæsthesia; on the forehead this pressure-border practically coincided with the border for cutaneous anæsthesia; on the cheek a progressive and symmetrical divergence of the borders always occurred with increasing pressures; the feeling of vibration everywhere within the anæsthetic zone was always less than, or different from, that on the sound side; but this might in part have arisen from the absence of cutaneous sensibility, but localization of every degree of perceptible pressure was almost invariably faulty immediately the zone of cutaneous anæsthesia was entered.

We therefore consider that the area of cutaneous anæsthesia and the area of anæsthesia to all pressures as high as at least 20 gm./dm.² are identical in the regions affected by the removal of the Gasserian ganglion, of the second and third roots, or of the second root only.

As regards higher pressures, our methods were not exact enough to afford accurate results. The investigation needs to be repeated with an instrument such that the rate at which the pressure is applied will be uniform, and will not vary as it does when pressure is exerted by weights; and in such a way that the scalp pressed against the head support can obtain no clue to pressure exerted on the face. Some degree of touch-perception of major pressures is, however, indubitably retained. The sensitive scalp against the head support might appreciate such higher pressures, but with a constant stimulus, such as 65 gm./dm.², the distribution of the sensitive areas is so irregular—little islets in the midst of the anæsthetic region—and the localization of perceptible stimuli, although inexact, is so evident that clearly a crude sense of pressure persists. This localization is not attained by tension upon the adjacent sensitive skin, for the point to which a pressure is mis-referred is usually in the zone of light touch anæsthesia, and seldom upon healthy areas; and in parts remote from the border of the zone the direction of misreference is not commonly towards the nearest

normal part. The degree of the persistence of this pressure-sense, and of the power remotely to localize, varied considerably.

III. LOCALIZATION, THE COMPASS-TEST AND THE POWER OF APPRECIATING VIBRATION.

To test the power of localizing pressure-touch, the patient with head supported and eyes closed was required at once to point to the spot pressed and was not allowed to grope. Within their respective anæsthetic areas the power to localize 2, 10, 20, and 65 gm./dm.² pressures was completely lost. To test the localization of greater pressures

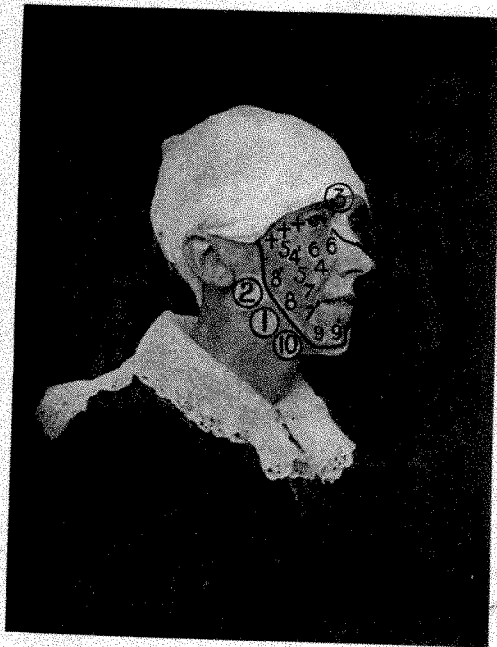


FIG. 3.

Case 12.—Section of the second and third roots of the fifth nerve. To show localizing power: correct references encircled; number represents the spot pressed; number with dash the misreference.

a perceptible but variable and unmeasured stimulus was obtained by the use of the algometer. Care was taken to keep well below the pressure-pain threshold. The localization of perceptible pressure-touch within the zone of light touch anæsthesia was almost invariably faulty (fig. 3). The extent of the misreference was inconstant; it was usually

least on the side of the nose and less about the chin and angle of the mouth than elsewhere; even on the same site with approximately the same stimulus it varied from time to time. The direction of the mis-reference was also variable; it was noteworthy that the localization was not usually towards the nearest normal area (fig. 4).



FIG. 4.

Case 20.—Extirpation of the Gasserian ganglion. To show localizing power. Correct references encircled; number represents the spot pressed; number with dash, the mis-reference.

In addition to the perception and localization of pressure-touch the discrimination of one from two points and the sensibility to vibration were also investigated. To apply two points of the compasses simultaneously with equal pressure on the face demands much practice. Here the difficulty was increased, for the compasses had to be applied over an area which was proved to be not uniformly anæsthetic to pressure. Usually on the forehead, however, and in some cases on the cheek also, we found that the power to discriminate one from two simultaneous points was either entirely lost, or greatly diminished. And yet the contact of two compass-points applied one after the other rapidly could be appreciated. The following record, taken from Case 20, shows

that although each separate contact was appreciated as a touch, the simultaneous application of the two points was never recognized as a double stimulation. The compasses were applied to the cheek, in front of the ear, immediately within the zone of cutaneous anæsthesia. The two points were separated for a distance of 4 cm. The figure 1 signifies that the patient answered that he was touched with one, 2 that he was touched with two points.

Stimulus				Answer			
One point	..	..	111	1111	11	1	
Two simultaneous points	..	1111	11	11	11		
Two consecutive points	..	222	22	22	22	2	

The proximity of the auditory apparatus and the sound-conducting properties of the facial bones prevented us from marking out the area of anæsthesia to vibration. The tuning-fork we used oscillated 128 times per second. It was first applied to the patient's hand so as to accustom him to the perception of vibration. In testing the face, the cheek was lifted off the bones by the examiner's finger; on the sound side no difficulty was then experienced in discriminating between the hearing and the feeling of vibration. Any stimulus strong enough to be perceptible to the supporting finger was easily appreciated by the patient. The affected cheek thus tested was usually quite insensitive, and if a fold of the anæsthetic skin was pinched up no feeling of vibration was perceived by it. Usually in the eye and rarely in the tongue was the loss complete; in the tongue, as a rule, some perception of vibration remained. The sensibility varied from time to time; on a subsequent day, with the same vibration-rate, in the same area, a partial might be substituted for a total loss. In all cases in which vibration was perceived on the affected side, it was invariably described as weaker than, or different from, the same stimulus on the sound side.

IV. PAINFUL PRESSURE.

For investigating pressure-pain on the face we used the Cattell algometer; but its formidable appearance, its tendency to slip, and its coarse adjustment made it unsuitable in so sensitive an area. A preliminary series of tests was made on the hand to reassure and to educate the patient. The algometer was then applied to the face without haste or jar, and by the examiner's left thumb and index the position of the point was so controlled as to obviate slipping. In testing the cheek one of us placed a finger on the oral surface, so as

to sustain the pressure of the algometer and to prevent all contact with the cranial bones; by this means we were able to examine the sensibility of the muscles alone. To produce pressure-pain in the tongue and eye, only the fingers were used: the whole thickness of the tongue was gripped between the thumb and index, and through the closed lids the eye was pressed back against the orbit.

Each of us examined the patient at all sittings, and made three tests at every site. As each had acquired with the algometer a rate and evenness of application which were a personal constant, we obtained, individually, results under uniform experimental conditions. The values recorded by R. F. K. were usually not identical with those by W. J. M., and thus the figures were not an absolute measure of the sensibility of a site to pressure-pain; but the relation of the sensibility at various sites, found by both observers, was uniform. The results at each sitting were thus controlled, and subsequent re-investigations provided a further check.

By cocainization we found that the skin of the normal face could be rendered insensitive to pinprick, von Frey's No. 4 hair, and low degrees of pressure-touch, without appreciably diminishing the sensibility to pressure-pain, as tested by the algometer.

The sensibility to pressure-pain within the area of superficial anaesthesia produced by intracranial operations on the fifth nerve varied over different regions in the same person, in different cases, and at different periods. Immediately after the section of the second root (Case 2) there was severe loss on the cheek, eye, and tongue; whereas six weeks later when the tongue and face had practically recovered, the eye remained insensitive. Case 12, after section of the second and third roots, showed almost complete loss on the eye and tongue, with less on the face; a fortnight later pressure-pain was still wholly lost on the eye, but only partially on the tongue and face. In a similar lesion six months old (Case 13) pressure-pain was normal except in the eye. In these two cases the motor supply to the frontalis had been cut in the skin incision, but pressure-pain in the forehead remained unaffected. In eight cases the Gasserian ganglion had been removed one to six years before our examination; in all the pressure-pain in the eye was absent or much diminished. In Case 15 (with a paralysed frontalis) and in Case 16 the pressure-pain elsewhere was normal; in Case 18 its threshold on the affected forehead was 6 kilos, whereas on the sound forehead it was only $\frac{1}{2}$ to 1 kilo; in Case 20 (fig. 6) the threshold on the affected forehead was 4 to 6 kilos, on the normal side 1 to $1\frac{1}{2}$ kilos. In

Case 19 (fig. 7) the frontalis was paralysed, and the pressure-pain threshold on the affected forehead was 6 to 9 kilos, on the normal 1 to $1\frac{1}{2}$; this patient also showed slight loss on the cheek and tongue. Cases 14, 17 (fig. 5), and 21 showed loss most pronounced over the forehead, but clearly demonstrable over the whole facial area of the fifth; and the last two had partial loss on the tongue also.



FIG. 5.

Case 17.—Extirpation of Gasserian ganglion. To show pressure-analgesia especially on the forehead. The numbers represent the pressures per unit area, in kilos.

On re-examining Cases 17 and 20 some days after they had first come under our observation, we found in the affected area marked tenderness and slight pain, which arose, the patient alleged, "from cold." The pressure-pain threshold that had previously been high was then so low as to reach almost the normal level; but, later, after the pain had passed, the tenderness disappeared and the first results were corroborated.

Of the ten cases of seventh nerve palsy, the following six showed no affection of the pressure-pain sense:—

Case 1.—Examined May, 1910. J. H., male, aged 41. Sudden complete left facial palsy of five weeks' duration, without affection of taste or hearing

(hearing was considered unaffected if the Weber and Rin  tests gave normal results); no reaction to faradism; typical reaction of degeneration; common sensibility everywhere normal; perception and localization of pressure-touch, vibration, discrimination of one from two points, and pressure-pain unaffected.

Case 2.—Examined May, 1910. E. Y., male, aged 7. Right facial palsy, dating from birth; no loss of taste nor hearing; no sixth nor other cranial nerve palsy; typical reaction of degeneration, no response to medium faradization; no loss of common sensibility; pressure-touch, vibration, point discrimination, and pressure-pain normal.

Case 3.—Examined May, 1910. Under care of Dr. Grainger Stewart. E. B., female, aged 37. Complete right facial palsy subsequent to mastoid operation for middle ear disease in January, 1908. Mr. Sargent, in October, 1909, divided affected facial after its exit from the stylo-mastoid foramen, divided also the hypoglossal of the same side, and sutured the distal end of the facial to the proximal end of the hypoglossal. On examination, the right side of the face was found still to be paralysed, the upper part being less affected than the lower; some deafness on right side; atrophy of right half of tongue with loss of taste; no reaction to medium faradization, reaction of degeneration well marked; no loss of common sensibility; no loss of pressure-touch, vibration, discrimination of one from two points, nor of pressure-pain.

Case 4.—Examined April, 1910. F. E., male, aged 38. Chronic right otorrh a, with slight deafness, right facial palsy, no loss of taste; paralysis more marked in lower than in upper face; no response to medium faradization, typical reaction of degeneration in upper and lower facial muscles; no loss of common sensibility; pressure-touch, vibration, and compasses normal; pressure-pain everywhere normal.

Case 5.—Examined May, 1910. J. H., male, aged 43. Left facial palsy, taste diminished, hearing unaffected; sudden onset exposure to cold. October, 1908: no faradic reaction, reaction of degeneration; common sensibility and pressure-sense everywhere equal on both sides.

Case 6.—Examined May, 1910. W. H., male, aged 34. Cold in the head for one week, April, 1910; then sudden onset of left facial palsy; upper part less affected than lower; taste much diminished; hearing unaffected; no faradic response, reaction of degeneration; inconstant diminution to pinprick in area of left fifth; pressure-touch perception and localization perfect; vibration slightly weaker on affected side; discrimination of two points normal; threshold for pressure-pain equally raised on both sides of the face, about 1 kilo above normal.

The remaining four cases of seventh nerve palsy all showed some affection of the pressure-pain sense.

Case 7.—Examined April, 1910. M. W., female, aged 63. Pain behind right mastoid for three weeks in January, 1910; then sudden loss of power in right face, and loss of taste without affection of hearing; complete loss to faradization, with typical reaction of degeneration; no loss to von Frey's No. 4 hair; perception and localization of pressure-touch vibration, and

discrimination of points equal on both sides; pressure-pain threshold over affected half of forehead, 3 kilos; over normal half, 1 kilo; elsewhere, approximately equal on both sides.

Case 8.—Examined April, 1910. M. S., female, aged 21. Left facial palsy with loss of taste but with hearing unaffected: sudden onset from exposure to cold in 1906; no response to faradism reaction of degeneration; no loss of common sensibility; pressure-touch normally perceived and localized; vibration and discrimination of points normal; on the affected forehead pressure-pain higher than on the normal; elsewhere, equal.



FIG. 8.

Case 9.—Left facial palsy from a basal fracture. To show pressure-analgesia over the affected muscles. The numbers represent the pressures per unit area, in kilos.

Case 9.—Examined May, 1910. G. W., male, aged 31. Basal fracture on March 5, 1910, produced left facial palsy, left deafness and loss of taste; galvanic tests for forced eye movements—electrodes* to meatus—reaction present on both sides, but very weak on left and very strong on right (Mr. Scott's note); slight response to medium faradism in orbicularis palpebrarum only; typical reaction of degeneration; no loss of common sensibility; pressure-touch perfectly perceived and localized; vibration less on left than on right, but difference not marked: points accurately discriminated; pressure pain showed marked loss over the facial muscles, equal on forehead and cheek, less on the chin (fig. 8); but was only slightly affected over subcutaneous bony points, and was normal on the eye and tongue.

Case 10.—Under care of Dr. Ormerod. Examined April and May, 1910. A. D., male, aged 34, pain in right mastoid region and fever for a week in 1905; then sudden right facial palsy with giddiness and loss of taste, but without affection of hearing; skin over affected forehead and cheek showed trophic and vascular changes; slight response to medium faradization in buccinator and in lower orbicularis palpebrarum, when tested through the skin in the usual way; but during the operation maximum faradization applied to the distal end of the divided nerve caused no muscular movement; typical reaction



FIG. 9.

Case 10.—Right facial palsy of acute inflammatory origin. To show pressure-analgesia over the affected muscles. The numbers represent the pressures per unit area, in kilos.

of degeneration; no loss of common sensibility; pressure-touch normally perceived and localized; vibration felt less on left than right; discrimination of points normal; pressure-pain much diminished on muscle-clad parts of the face; loss approximately equal on cheek and forehead: less loss on bony points (fig. 9); slight inconstant diminution in affected half of tongue also. Mr. Sargent divided the affected facial and the hypoglossal on the same side; sutured the proximal end of the hypoglossal to the distal end of the facial; electrical changes appeared in the tongue within twenty-four hours and the tongue muscles duly began to atrophy; in the face no loss of common sensibility, no loss of pressure-touch, nor further loss of pressure-pain occurred

after the operation; in the tongue absolutely no further sensory changes could be detected.

The following are the average relative pressures required to elicit pain over the various sites in these last four cases:—

Site	CASE 7		CASE 8		CASE 9		CASE 10	
	Paralysed side	Sound side	Paralysed side	Sound side	Paralysed side	Sound side	Paralysed side	Sound side
Forehead	3	1	$2\frac{1}{2}$	$1\frac{1}{4}$	$3\frac{1}{3}$	$1\frac{1}{8}$	4	$1\frac{1}{4}$
Ext. ang. process ..	1	1	$\frac{1}{2}$	1	$1\frac{1}{2}$	1	$2\frac{1}{2}$	$1\frac{1}{2}$
Zygoma	1	$\frac{1}{2}$	1	1	$1\frac{1}{2}$	1	$1\frac{1}{2}$	1
Malar region	1	$\frac{1}{2}$	1	$1\frac{1}{2}$	$3\frac{1}{2}$	$\frac{1}{2}$	4	1
Cheek	$1\frac{1}{2}$	$1\frac{1}{2}$	$1\frac{1}{3}$	1	$3\frac{1}{2}$	1	4	$1\frac{1}{2}$
Chin	1	$1\frac{1}{2}$	$1\frac{1}{2}$	$1\frac{1}{2}$	1	1	2	1
Angle of jaw	$1\frac{1}{2}$	$1\frac{1}{2}$	$1\frac{1}{2}$	$1\frac{1}{2}$	—	—	$1\frac{1}{2}$	$1\frac{1}{2}$

Ionization of a 10 per cent. solution of cocaine by means of a current of 10 to 20 milliampères, for a period not exceeding twenty minutes, over the areas in which pressure-pain was diminished, did not further depress the sense.

Of the two cases of intracranial tumour, one, Case 22, presented a partial fifth and seventh palsy without loss of pressure-pain in the eye, face, or tongue; the other, Case 23, who was somewhat demented, had complete paralysis of the fifth and seventh with disintegration of the affected eye; her pressure-pain threshold over the whole fifth area was at least 5 kilos; the loss, though definite, was not so well marked on the tongue.

Cases 1 to 6 show that complete section of the trunk of the seventh nerve distal to the stylo-mastoid foramen may occur without influencing sensibility to pressure-pain; and that lesion of the seventh, where it is associated with the chorda tympani, may occur at any level as high as the entrance of the seventh into the middle ear without affecting pressure-pain, and without impairing the general sensibility in the face. In these six people the seventh nerve after its emergence from the Fallopian canal contained no fibres subserving deep sensibility. But Cases 7, 8, 9 and 10 conclusively prove that injury to the seventh nerve may be associated with very definite loss of pressure-pain. In Case 9 the deafness and the diminished response to the galvanic test for forced eye-movements, and in Case 10 the giddiness, pointed to involvement of the eighth nerve, and indicated that the lesion to the seventh occurred in the Fallopian canal. Now we have shown that in cases where we were certain the seventh lesion lay outside the Fallopian canal, there was no loss of pressure-pain, and that with a lesion in the canal pres-

sure-pain was lost to a certain degree. The seventh nerve is therefore probably joined by these sensory fibres as it lies in the canal. And from Cases 7 and 8 it seems as if the sensory fibres from the forehead come earliest into relation with the motor trunk; or in the canal they may be the most superficial of the pressure-pain fibres and thus the most liable to be involved in inflammatory processes. In Cases 9 and 10 much loss of pressure-pain could be demonstrated in the presence of a normal fifth and desensitizing the skin did not increase the loss. In both the loss was observed practically only on the forehead and on the cheek. Bony parts, such as the zygoma and the external angular process, showed at most merely a slight loss. The pressure-analgesia was therefore almost exclusively confined to the region of the facial muscles.

The Cattell algometer, as we used it, was useless for testing the pressure-pain sense in the skin, for its application necessarily involved pressure on the subjacent tissues. Our experiments upon the effect of desensitizing the skin proved only that the subjacent structures had a degree of pressure-sensibility not appreciably less than that of the skin. It is ridiculous to suppose that the crude sensibility that remained in these lesions of the seventh nerve represented the sensitivity of the skin, for if pressure-pain organs of the skin do not respond to pressures appreciable when applied to normal muscle their existence is purposeless. But as the loss was confined to muscle-clad areas the skin over the facial muscles must have a pressure-pain sense whose fibres also were involved in these seventh injuries.

The degree of loss was the same over the frontalis pressed against the frontal bone as in the buccinator pressed against a supporting finger on its oral surface. It seemed most unlikely that the thin muscular layer of the frontalis, in spite of its degenerated condition, was still able to intercept all pressures directed against the subjacent bone. A few trials of interposing varying thicknesses of blotting paper and soft leather between the point of the algometer and the normal skin showed that a layer of approximately the same thickness as the frontalis could not possibly make a difference of 3 kilos in the pressure required to produce pain. The fibres from the frontal bone must therefore have been affected to the same extent as the fibres from the frontalis. These pressure-pain fibres which join the seventh therefore must certainly convey impulses from the facial muscles, very probably also from the bones upon which these muscles lie, and less surely from the skin over them.

The threshold in Cases 9 and 10 both over the forehead and the cheek was raised to between 3 and 4 kilos. In each the seventh was injured in the Fallopian canal, and each had lost the same sense to practically the same degree. As in both cases the threshold over the whole facial muscular area was practically equal, all the pressure-pain fibres in the Fallopian canal associated with the seventh nerve had probably been destroyed; for although coincidence might explain the equality of the loss on the cheek and the forehead in one case, it could scarcely be due to chance when two cases, one of traumatic the other of inflammatory origin, showed the same phenomenon. Each of these cases had, therefore, apparently lost the same bundle of fibres; a bundle whose function is essentially distinct from the sensory functions of the fifth, is not influenced by the cocaineization of the cutaneous filaments of the fifth, and cannot (Case 10) be subserved by the fifth; a bundle which is not associated with the peripheral seventh after the seventh enters the middle ear; a bundle which is concerned almost exclusively with the pressure-pain sense in the muscular apparatus of the face; a bundle which has a functional and not a topical distribution.

Immediately after intracranial interference with the fifth, the pressure-pain sense was tremendously affected; over the malar region in Case 11 the threshold rose to 6, and in Case 12 to 10 kilos. As the seventh acquires from the facial muscular apparatus pain-fibres which conduct impulses from pressures up to 4 kilos, the sudden injury in the region of the fifth roots must have completely deranged the functional activity of these sensory fibres; and as sometimes the loss in the muscular areas was permanent, the fibres which join the seventh in the Fallopian canal must first enter the region of the fifth roots. As in Case 12 the pressure-pain sense within a fortnight was practically normal, again this recovery of function must have been independent of regeneration of destroyed nerve-fibres. The completeness of recovery must be in part at least regulated by the degree of integrity of these fibres to the seventh; and in cases such as 11, 12, 15, and 16, in which the pressure-sense returned to normal, these fibres probably escaped irreparable damage; and the duration of their convalescence may be an index to the degree to which they were injured.

The extent of the field of operation probably varied in different cases, but an arrangement which thus permits pressure-pain fibres destined for the seventh to associate first with the fifth may also permit variations in the rate and level at which these fibres leave the fifth. The greater the number of these pressure-pain fibres which entered the

vicinity of the Gasserian ganglion before passing to the seventh, the fewer would escape injury, and the greater would be the permanent loss of pressure-pain.

But varying affections of these fibres alone could not explain the recovery over the zygoma and external angular process and could explain adequately the different degrees of recovery upon the forehead, cheek, and chin, only if the permanent loss was not greater than the upper limit of the threshold of pressure-pain impressions conveyed by them. This limit we have shown is probably about 4 kilos; but in Case 14 the threshold was permanently maintained at 9, in Case 17 at 8, in Case 19 at 9, and in Case 20 at 6 kilos, over isolated areas upon the forehead (figs. 5, 6, 7). In these cases the fibres which join the seventh from such areas must be entirely destroyed with the fifth; some other crude mechanism must be involved, and must be affected in varying degree in different cases.

A year or more after the removal of the Gasserian ganglion the degree of recovery varied considerably. Twice (Cases 15 and 16) no loss could be detected—but we did not here exclude the possibility of permanent loss affecting the skin. But in all the others some degree of impairment of pressure-pain was demonstrable.

The constancy, severity, and permanency of the loss in the eye indicated that its pressure-pain fibres were invariably and almost wholly concentrated within the field of operation. The result was the same in our three cases of root lesions as in the cases of Gasserian removal, except that in the root cases some pain-sense was always present, whereas in the ganglion cases, although pain on great pressure sometimes persisted, sometimes all sensibility was lost. Some pressure-pain fibres undoubtedly sometimes escaped. Unfortunately in our only case of complete central fifth lesion the affected eye had been removed. We were, therefore, unable to prove whether the fifth really subserved pressure-pain in the eye or whether the results were due to injury of the pressure-pain fibres on their way through the region of the fifth roots to some destination other than the fifth. The fibres found associated with pressure-pain impulses in the seventh conveyed no impulses from the eye.

Except on the eye we never met such absolute loss as is sometimes seen in tabes, where only regard for the integrity of the tissues limits the threshold. Thus obviously some pressure-pain fibres from the facial area must never enter the region of the fifth roots.

The loss on the cheek was constantly less than on the forehead; the

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lips always suffered less than the cheek ; the cheek was never affected if the forehead escaped ; and the tongue enjoyed greater immunity than any other site.

Sometimes the forehead alone, for example in Cases 19 and 20 (figs. 6 and 7), showed loss. This result was not due to the cutting of fibres of the peripheral seventh in the skin incision, for we have already proved that the seventh after its emergence from the Fallopian canal usually contains no sensory fibres ; the threshold in these cases was invariably above the limits of the fibres going to the seventh ; and in Case 15, where a combined fifth and seventh palsy was present on the forehead, pressure-pain was normal.

We have already proved that a loss with a threshold of 4 kilos over the muscle-clad areas of the face must be due to injury to a crude pressure-pain mechanism. As the forehead was most frequently affected, and as any loss on the forehead was always above this threshold, its pressure-pain fibres belonging to this crude mechanism must be most often exposed to injury in the field of operation. And as over the forehead the loss was never uniform, but sometimes varied in its threshold in the same case as much as 4 kilos, this crude mechanism must have a rich network of anastomoses affording alternative paths from the same area.

In no case over any site other than the forehead was the threshold higher than 5 kilos. In Case 17, for example (fig. 5), the threshold on the forehead was 7 kilos ; on the zygoma, 5 ; on the cheek, 4, and on the tongue, less. The fibres of this crude mechanism, which from other sites enter the fifth root area, are thus very much fewer than those from the forehead. The above figures are an index to their relative numbers in this case. Such fibres in the fifth root area are derived mainly from tissues in the immediate vicinity.

V. SENSATIONS OF PRESSURE IN THE TONGUE.

With the pressure-sense of the tongue the peripheral hypoglossal appears to have no concern. In Cases 3 and 10 the hypoglossal nerve was completely cut across and the ends so manipulated as to render re-establishment of continuity impossible. Electrical changes appeared in the affected muscles on the second day, and atrophy duly developed. There was absolutely no alteration of the pressure-pain sense nor evidence of any sensory loss in the affected half of the tongue at any time after the division of the hypoglossal ; if the distal portion carried

any afferent fibres they must have left the nerve before the level of the section. Pressure-pain fibres may join the hypoglossal proximal to the level of the section, but in a case of mal-development of the tongue of central origin, the rudiment possessed normal sensibility. The twelfth nerve in these two cases conveyed neither pressure-pain nor other sensory impressions; it is probably a pure motor nerve in its peripheral course.

In Cases 3, 5 and 6, in which unilateral loss of taste resulted from destruction of chorda tympani fibres in injuries to the facial nerve after its emergence from the Fallopiian canal, no difference between the pressures necessary to elicit pain in the right and in the left half of the tongue was detected; in all tactile sensibility was unimpaired. In Cases 7, 8, 9 and 10 unilateral loss of taste existed; as pressure-pain in the face was affected in all, the lesion was probably in the Fallopiian canal, but only in Case 10 was there any loss on the tongue, and it was slight. The pressure-pain fibres from the tongue do not pass in the chorda tympani.

The effect of intracranial fifth lesions upon the pressure-pain in the tongue closely resembled the effect already discussed in connexion with the face. Immediately after operation the loss might be absolute, but recovery was rapid, and often complete; and the degree of loss which remained was inconstant and never severe. Here also, therefore, the results pointed to interference with some mechanism other than the fifth in the field of the operation; the crude pressure-pain mechanism already referred to always escaped appreciable injury, but a finer pressure mechanism was usually damaged.

In injury to the seventh in the Fallopiian canal, although the fifth was normal, pressure-pain over the muscular apparatus of the face had a threshold of about 4 kilos. In Cases 14, 17, 18, 19, 20 and 21, of removal of the Gasserian ganglion, as the pressure-pain threshold on the forehead was above 4 kilos, the fibres which go to the seventh must have been destroyed; the fifth was also gone, but pain was sometimes produced from severe pressure on the eye; on the face from 4 to 9 kilos always, and on the tongue a pressure of less than 4 kilos constantly evoked pain. In Case 23 pain was produced on the face from pressures above 5 kilos, on the tongue from less. Perception of these crude pressure-pain impulses can be, therefore, a function neither of the fifth nor of the seventh; its inconstant disturbance in intracranial operations upon the fifth nerve must depend upon the accidental disturbance of some mechanism whose fibres in varying numbers enter the operation zone.

The only nervous mechanism whose fibres are neither wholly nor essentially of the fifth; whose fibres are common to the eye, forehead, zygoma, cheek, lips, and tongue; whose fibres invariably occur in the region of the fifth roots and are there in greater proportion from the eye and forehead than from the cheek and tongue; whose fibres anastomose so perfectly that total isolated destruction at any one site is practically impossible; and whose fibres are so diffused that they can be involved in lesions in so many different regions: the only nervous mechanism which fulfils these conditions is the sympathetic, and it fulfils them adequately. The sympathetic must therefore subserve a pressure-pain function; it can conduct pressure-impulses which, at least from 4 kilos and upwards, are appreciated as pain; it is the mechanism of a primitive generalized pressure-sense which ignores the function of the area from which its fibres come.

VI. CONCLUSIONS.

The fibres conveying impulses from pressures, up to at least 20 gm./dm, we conclude, probably run in the peripheral branches of the fifth nerve, certainly are present in the roots of the fifth, and certainly enter the Gasserian ganglion. The fibres conducting the power to appreciate and to localize crudely considerable pressures may travel in the fifth peripheral branches, but take another course before the confluence into roots, or may have an entirely different path completely independent of the fifth. In the cases in which the seventh supply to the forehead was cut in the skin incision during removal of the Gasserian ganglion, pressure-sensibility was affected in the same manner and to the same degree as in involvement of the fifth alone. But from the observations on pressure-pain it is certain that the seventh nerve and the sympathetic are alternative courses for impulses conveying some forms of deep sensibility. The existence of such by-paths implies the possibility of variations in their functional importance in different persons; hence the degree to which the pressure-sense persisted in different patients may in part have arisen from individual peculiarities in the relative proportion of the fibres subserving deep sensibility in the fifth, seventh, and sympathetic nerves. But whatever sensibility to pressure-touch may be subserved by fibres which do not enter the Gasserian ganglion, it has so high a threshold and so crude a localizing power, that the fifth must be regarded as the nerve which primarily and essentially conducts from the face area the impulses which in everyday life affect consciousness as pressure-touch.

It is more than probable that ordinary pressure-touch impulses go to the fifth nucleus, but we have not been able conclusively to determine this. The case of recovery after removal of a right extra-cerebellar tumour had a unilateral complete fifth and seventh palsy. She showed loss of perception and localization of all pressures beneath those which reached her heightened threshold for pressure-pain. But she had suffered gross destruction of brain-tissue and was not a good witness. The other extra-cerebellar case had not wholly lost her cutaneous sensibility over the affected fifth area, yet pressure-touch seemed to share in the general raising of the threshold of sensitiveness to stimuli. The observations, unfortunately, were made once only, as the fifth and seventh palsies appeared suddenly, and the patient was at once operated upon.

The whole fifth area receives from the superior cervical ganglion sympathetic fibres, which are chiefly distributed along the vascular paths, mainly of the internal carotid; the principal vascular branches to the eye and forehead arise within a restricted area, which is within the field of every Gasserian ganglion operation. The principal sympathetic supply to these regions is derived from the carotid and cavernous plexuses; all the eye and forehead fibres are practically within the danger zone, and hence the frequency, severity, and permanency of loss of pressure-pain over these sites probably depends on injury to these sympathetic fibres. The ramifications of the vascular supply to the rest of the face and to the tongue afford innumerable channels for the sympathetic; from these remoter regions also fewer fibres pass to the plexuses in the vicinity of the Gasserian ganglion; this may be the explanation of the greater immunity of the crude degree of the pressure-pain sense of these areas.

The seventh lesions show that the more sensitive mechanism is in intimate association with the nerve which subserves the particular function of the area from which its fibres are derived. The fifth lesions show that these low threshold fibres, at any rate from the facial muscular apparatus and eye, and probably also from the tongue, are concentrated in the neighbourhood of the fifth roots before passing to their ultimate destination. The permanent loss which sometimes persisted after fifth nerve lesions only on the forehead suggests that the sensitive fibres from the muscles leave the fifth root region probably by branches at different levels. Their functional grouping is evident in the Fallopiian canal; the loss persists in approximately the same degree in our single case of nuclear lesion; all the muscular sensory

fibres probably proceed centrally by way of the Fallopian canal. None of these fibres pass by the peripheral branches of the seventh; there was no evidence regarding their relation to the peripheral branches of the fifth; but if none pass in the fifth branches, how do these muscular pressure-pain fibres concentrate in the region of the fifth roots? We consider that their probable course is from the skin, muscles, and bones, which comprise the facial muscular apparatus, by the terminal branches of the fifth, and by the blood-vessels to the fifth root region; thence by way of Meckel's ganglion, Vidian nerve, great superficial petrosal, to the geniculate ganglion; thence by the pars intermedia, a nerve whose fibres have a very small calibre, to the fasciculus solitarius and region of the facial nucleus. But some may also pass by the otic ganglion and small superficial petrosal.

Only in a certain section of its course does the seventh contain afferent fibres. Our knowledge of the approximate site of entry of these fibres, and of the purely motor function of the seventh after it leaves the Fallopian canal, and of its sensory functions proximal to this point, may now prove an aid to the localization of lesions of the seventh. As the pressure-pain sense may exist unimpaired over the muscles after electrical responses have disappeared, its observation may have a prognostic value also. In Case 10 there were profound vascular and trophic changes associated with the destruction of pressure-pain fibres. Whether such muscles devoid of these fibres are capable of recovery requires proof: the hypoglossal appears to be a purely motor trunk, and probably cannot supply these lost trophic fibres. Perhaps facial palsies which show pressure-pain loss might be better exempted from anastomotic operations till a little more is known about their nutritive capability.

Injury to any of these low threshold fibres seems to be irreparable, for in Case 10 their destruction in the muscular apparatus was associated with slight loss on the bony points and on the tongue, and in all these areas the loss persisted for five years in the presence of a normal fifth; in this connexion also the constancy and severity of the loss on the eye is noteworthy.

The eye, tongue, and face also possess this low threshold pressure-pain mechanism, but we have no evidence of the course its fibres take from these areas, except that they share in the general concentration in the fifth root region.

The difference between these two pressure-pain mechanisms is that the one has a low threshold and a functional distribution, the other

has a high threshold, and subserves a general sense without relation to the particular local function of the area from which its fibres come. Has the finer sense been elaborated from a general pressure-sense? Does the finer mechanism consist of specialized sympathetic fibres? Is deep sensibility subserved everywhere by a common mechanism, which is elevated in special areas in adaptation to the requirements of local function?

Dr. Henry Head and Dr. Gordon Holmes taught us the methods of investigation we used. We wish the paper was more complete, more worthy of the aid we received from them.

We are indebted to the Medical Committee of the National Hospital for permission to publish all except one of our cases; we gratefully acknowledge their kindness.

VII. SUMMARY.

(1) The fifth nerve must be regarded as the essential path for those impulses from the face which affect consciousness as sensations of *pressure-touch*.

(2) After removal of the Gasserian ganglion *pressure-pain* may persist unimpaired in the face and tongue, but never in the eye.

(3) The seventh nerve contains no pressure sense fibres distal to the Fallopian canal.

(4) The seventh nerve in the Fallopian canal is associated with pressure-pain fibres (low threshold mechanism) conveying impulses from pressures up to about four kilos, from the skin muscles and bones of the facial muscular apparatus.

(5) These low threshold pain fibres pass through the region of the fifth roots before entering the Fallopian canal.

(6) The sympathetic subserves a general crude sensibility to pressure-pain (high threshold mechanism) which, sometimes, may persist alone after removal of the Gasserian ganglion.

(7) The peripheral twelfth was not found to convey any form of sensation to the tongue.

CASES TO WHICH ALLUSION HAS BEEN MADE IN THIS PAPER.

Case 11.—J. C., female, aged 53. Under care of Dr. Collier. Mr. Armour cut second root, April, 1910. Examined March to May, 1910.

Case 12.—Mrs. MacD., aged 40. Under care of Dr. Tooth. Mr. Sargent cut second and third roots, April, 1910. Examined April and May, 1910.

Case 13.—H. E., female, aged 45. Under care of Dr. Turner. Sir Victor Horsley cut second and third roots. September, 1909. Examined February, 1910.

Case 14.—R. P., male, aged 63. Under care of the late Dr. Beevor. Removal of Gasserian ganglion by Sir Victor Horsley, March, 1908. Examined February to May, 1910.

Case 15.—E. B., female, aged 35. Under care of Dr. Risien Russell. Removal of Gasserian ganglion by Sir Victor Horsley, July, 1908. Examined February, 1910.

Case 16.—E. D., female, aged 49. Under care of Sir William Gowers. Removal of Gasserian ganglion by Sir Victor Horsley, February, 1908. Examined March, 1910.

Case 17.—B. S., female, aged 36. Under care of Dr. Risien Russell. Removal of Gasserian ganglion by Sir Victor Horsley, March, 1907. Examined February to March, 1910.

Case 18.—I. C., female, aged 56. Under care of Sir David Ferrier. Removal of Gasserian ganglion by Sir Victor Horsley, April, 1905. Examined March, 1910.

Case 19.—F. B., male, aged 50. Under care of Dr. James Taylor. Removal of Gasserian ganglion by Sir Victor Horsley, December, 1904. Examined January, 1910.

Case 20.—S. C., female, aged 53. Under care of Dr. Risien Russell. Removal of Gasserian ganglion by Sir Victor Horsley, December, 1904. Examined March, 1900.

Case 21.—J. G., male, aged 56. Under care of the late Dr. Beevor. Removal of Gasserian ganglion by Sir Victor Horsley, September, 1905. Examined January, 1910.

Case 22.—Mrs. C., aged 34. Under care of Dr. Turner. Removal of large left extra-cerebellar tumour by Mr. Sargent, March, 1910. Examined February and March, 1910.

Case 23.—Miss T., aged about 50. Right ? cerebellar tumour removed by Mr. Ballance fifteen years ago. Examined by the courtesy of Dr. J. R. Lunn, Medical Superintendent of St. Marylebone Infirmary, May, 1910.

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DISPLACEMENT OF THE CEREBELLUM FROM TUMOUR OF THE POSTERIOR CRANIAL FOSSA.¹

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I DESIRE to call attention in this paper to two forms of displacement of the cerebellum as a result of tumour of the posterior cranial fossa—viz., the lateral displacement, in which the cerebellum is nearly at a right angle with the brain-stem; and the upward displacement, in which the tentorium is much distended and the occipital lobes are widely separated by the dislocated cerebellum.

Displacement of the cerebellum from tumour of the cerebello-pontile angle so that the cerebellum is twisted greatly toward one side is of unusual occurrence. In my collection of nine large tumours external to the cerebellum, in or near the angle mentioned, extreme lateral displacement resulted only twice. I do not include in this number tumours seen at operation, or intracranial tumours that developed in the region of the trigeminal nerve, or tumours in the cerebellum. Usually atrophy of the parts about a tumour is produced when the pressure is intense, and twisting of the cerebellum is therefore less likely to occur.

The twisting of the cerebellum complicates operation for removal of a tumour of the posterior cranial fossa. The medulla oblongata becomes less resistant, and a fatal termination is more likely to follow operation than in cases in which less distortion of the medulla oblongata has occurred. The cerebrospinal fluid also may be increased, as in my Case No. 558, reported in this paper, and the escape of so large an amount of fluid produces very grave symptoms. The twisting of the cerebellum does not necessarily hasten death, although the effect on the vagus nerve from displacement of the medulla oblongata might be regarded as serious.

In Case 1 [No. 421] the symptoms of tumour first appeared about three and a half years before death. They became intense, and

¹ Read before the Philadelphia Neurological Society, January 27, 1911.

although the displacement of the cerebellum was great, the lateral twisting on the brain-stem was not so extreme as in Case 2 [No. 558], in which the symptoms were much less severe. In Case 1 the tumour was much larger than in Case 2, and it must have stretched the tentorium greatly, as it extended far enough forward to press upon the left oculomotor nerve. It also depressed the left occipital lobe. A deep depression of this part of the brain is a somewhat rare occurrence from

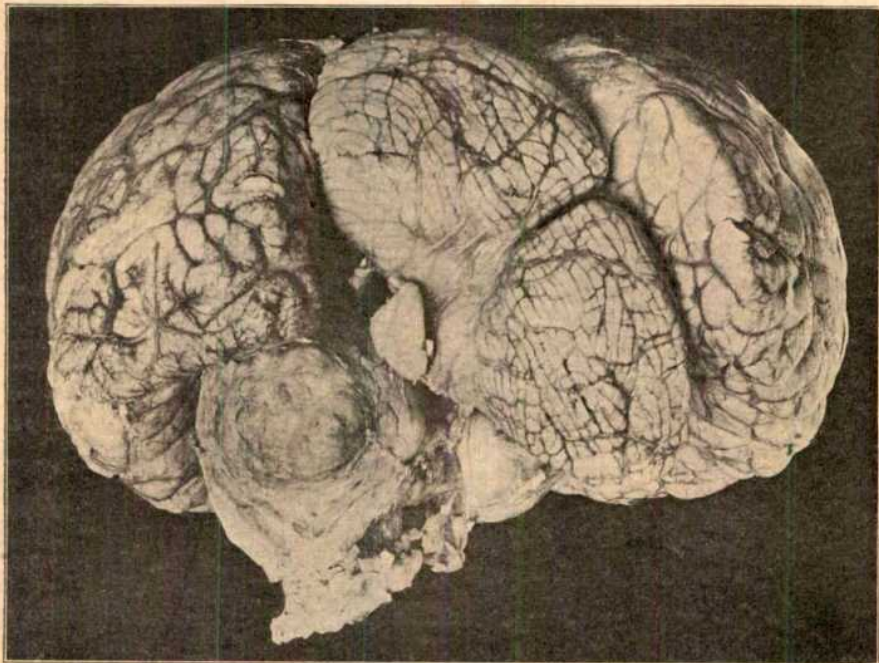


FIG. 1.

Case 1 [No. 421].—The occipital lobes are widely separated by the displaced cerebellum.

a subtentorial tumour. The displaced cerebellum separated the occipital lobes from one another, and the space provided in this way diminished the degree of lateral twisting of the cerebellum upon its axis. It is possible that during life the separation of the occipital lobes was not so great as is represented in fig. 1, as the tentorium, though greatly distended, must have afforded considerable resistance to pressure. A brief reference to this case with the photograph has been published in a previous paper by me in the *Journal of the American Medical Association*, vol. lii, No. 4, p. 278, 1909.

Two parts of the brain are especially affected by the distortion of

the cerebellum—viz., the pons at its union with the cerebral peduncles, and the medulla oblongata. If the pressure be from below upward with sufficient force to separate the occipital lobes and stretch the tentorium, as in Case 1, the lateral displacement of the cerebellum is less and the stretching of the medulla oblongata also is less. When the pressure is from one side and displaces the cerebellar lobes almost to a right angle with the brain-stem, as in Case 2, the stretching of the medulla oblongata is pronounced, and this part of the brain may be displaced as

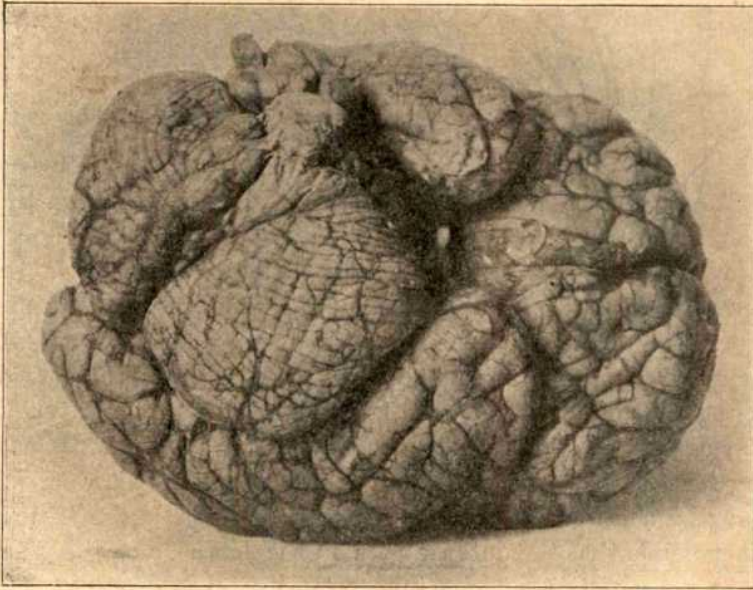


FIG. 2.

Case 2 [No. 558].—The tumour is on the right side, and has pushed the cerebellum to the left. The pons and medulla oblongata are displaced 3·5 cm. to the right (the side of the tumour) by the left lobe of the cerebellum.

much as 3·5 cm. Inasmuch as the medulla oblongata is continuous with the cervical cord, a dislocation of such a degree would cause stretching of the nerves arising from the former. In Case 2 the cerebellum was pushed to the left by the tumour, but the pons and the medulla oblongata were pushed by the displaced left cerebellar lobe to the right—i.e., to the side of the tumour—and the left side of the pons was much flattened by the pressure from the left cerebellar lobe.

In some instances symptoms have been observed indicative of a

lesion on the side opposite to that occupied by a basal tumour. An explanation has been sought in pressure upon the medulla oblongata on the side of the tumour, below the motor decussation, or in pressure of the pons and medulla oblongata of the opposite side against the base of the skull, or, more recently by Oppenheim, in the constriction of the medulla oblongata by the tightly stretched vertebral artery. Oppenheim has considered it possible that in lateral displacement of the pons and medulla oblongata, the pyramidal tract on the convex side of the arch—i.e., the opposite side to the tumour—may be more damaged. I am not aware that anyone has referred to stretching of cranial nerves on the side opposed to the tumour by the displacement of the pons and medulla oblongata from the median line in the direction of the tumour by a dislocated cerebellar lobe, or to pressure on the contralateral side of the pons by the displaced cerebellar lobe, as seen in Case 2.

The pain in Case 2 was described as unbearable, as of a pressing or burning character, and as though someone were pressing on the side of the head. It was situated in about the left motor region, but extended well into the left occipital region. Very little pain was felt in the left side of the face. The sensation was more one of burning than of pain. The supra-orbital and infra-orbital foramina were tender to pressure on both sides. In speaking, and voluntary drawing up the corners of the mouth, together or separately, the left side of the face was not moved so much as the right, but the inequality of the movement was slight. Hearing for the voice and watch was considerably impaired in the left ear, though much less than in the right ear.

It is possible that the intense pain in the left side of the head, the slight weakness of the muscles innervated by the left facial nerve, and the moderate degree of deafness in the left ear, were caused by stretching of the left trigeminal, facial, and acoustic nerves from the displacement of the medulla oblongata and pons 3.5 cm. to the right—i.e., toward the side of the tumour. This displacement was produced by pressure from the distorted left lateral lobe of the cerebellum, and is very different to the displacement referred to by Oppenheim, which is to the side opposite to the tumour.

It is uncertain whether headache can be caused by stretching of the trigeminal nerve. It seems at least possible, as the nerves of the cerebral dura, according to "Gray's Anatomy," are filaments from the trochlear, the ophthalmic division of the trigeminal, the semilunar, or Gasserian ganglion, the vagal, the hypoglossal, and the sympathetic. In Case 2, the supra-orbital and infra-orbital foramina on each side were

tender to pressure. The stretching of the left trigeminal nerve may have caused this tenderness on the left side, and the implication of the right trigeminal nerve in the tumour at its surface doubtless caused the tenderness on the right side.

One is impelled to ask why it is that lateral displacement of the cerebellum does not occur more frequently.

In a case of Dr. Mills' [No. 342] the tumour was very much larger than in Case 2, and was in the same situation, but it formed dense adhesions with the left cerebellar lobe and pons, and caused much atrophy of these parts. It did not cause any important displacement of the cerebellum. It was as firm a tumour as that in Case 2, and

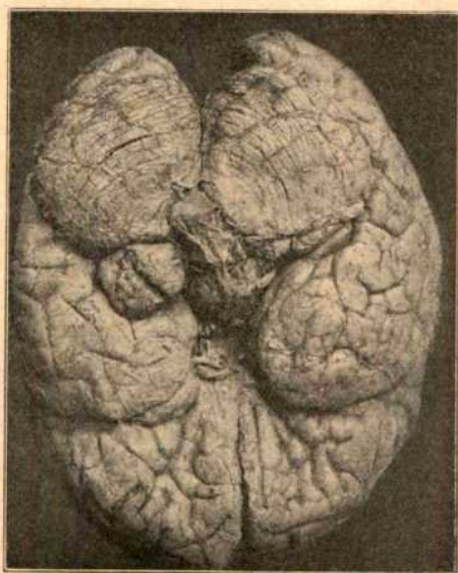


FIG. 3.

Case 3 [No. 205].—A small tumour having a similar origin to that in Case 2, but causing no displacement of the cerebellum.

grew in the same direction, along the margin of the cerebellar lobe. It caused moderate atrophy of the overlying occipital lobe. The adhesions of the tumour to the surrounding parts were much stronger than were those of Case 2, and probably in this fact lies the explanation of the absence of displacement of the cerebellum. The pressure on the cerebellum from so large a tumour (measuring 5.5 cm. antero-posteriorly by 3.5 cm. laterally) must have been greater than from the tumour in Case 2, therefore neither position nor size of the growth is sufficient alone to explain the greater displacement of

the cerebellum in Case 2, but between these two tumours a difference exists in the density of the adhesions between the tumours and the surrounding parts. If adhesions form early between the tumour and the cerebellum on one side, and the tentorium on the other, the likelihood of much displacement of the cerebellum is lessened, and atrophy of the parts about the tumour will occur. The cerebellum being bound to the tumour by dense adhesions resists displacement, and atrophies proportionately to the pressure from the tumour. Other factors are concerned, however, in the displacement of the cerebellum.

In Case 3 [No. 205], one of Dr. Mills', with whom I saw the patient (reference has also been made by Dr. Weisenburg to this case), the tumour was about the size of that in Case 2, was equally firm and equally well defined from the surrounding tissues. It occupied a very similar position, but, unlike the tumour of Case 2, it caused considerable atrophy of the overlying occipito-temporal lobe, this through the tentorium, and only moderate atrophy of the adjoining cerebellar lobe. This tumour measured 2.5 cm. antero-posteriorly by 3 cm. laterally, but where it arose from the cerebello-pontile angle it measured only 1.5 cm. The greater diameter was at its outer portion, where it sent a projection anteriorly which caused pronounced atrophy of the occipito-temporal lobe. The shape of the tumour as well as the atrophy of the occipito-temporal lobe, which could only have been produced by distension of the tentorium, indicates that the pressure from the tumour must have been chiefly forward.

The resistance afforded by the tentorium must be another factor in the displacement of the cerebellum; where the membrane is dense and unyielding, the pressure against the cerebellum is greater.

In Case 4 [No. 338], also one of Dr. Mills', the adhesions between the cerebellum and the tumour were very dense, and great atrophy of the cerebellar lobe on the same side and of this side of the pons occurred. The cerebellum had not been displaced laterally, although this tumour measured 5 cm. antero-posteriorly by 6 cm. laterally by 4 cm. from above downward. The pressure evidently was from below upward, for while only slight atrophy of the overlying occipital lobe had been caused, this occipital lobe had made a deep indentation in the upper part of the lateral lobe of the cerebellum on the side of the tumour by the pressure of the inferior and median edge of the occipital lobe, and the cerebellum had been pushed upward between the two occipital lobes, separating the occipital points as much as 6 cm. The pressure from the displaced cerebellum on the median

side of each occipital lobe must have been considerable, not so much, however, as in Case 1, where the occipital points were separated as much as 8 cm.



FIG. 4.

Case 4 [No. 338].—A much larger tumour than that in Case 2, and having a similar origin, but causing little displacement of the cerebellum.

In Case 5 [No. 296] where the patient was under my care the separation was even greater. A large tumour measuring 5 cm. antero-posteriorly by 6 cm. laterally by 5 cm. from above downward, developed in the cerebello-pontile angle, but its origin doubtless was from the dura at the base of the posterior cranial fossa. It was not adherent to the brain. The pressure being from below upward, it caused no lateral displacement of the cerebellum, but it drove the cerebellum far upward between the occipital lobes, separating the occipital points 9 cm. Such displacement as this, notwithstanding the intervening tentorium, gives a fair idea of the great pressure that must have existed, and suggests the possibility of occipital lobe symptoms from cerebellar tumour. As the displacement, however, cannot occur until the pressure from the tumour becomes great, and not until papilloedema has developed, hemianopsia could not be expected, and symptoms of occipital lobe lesion would be masked.

Condensed notes of the two cases selected as illustrative of the two forms of displacement described in this paper are as follows :—

Case 1 (laboratory number 421).—E. M., female, aged 20, was admitted to the Philadelphia General Hospital, May 1, 1907, and died January 8, 1908. Her sight had been poor since she was 7 years old. Frontal headache had existed about three years, but it had become much worse during the two months before her entrance in the hospital. Two weeks before any notes were taken she began to have difficulty in walking and in speaking. When she came to the hospital she was unable to walk or stand alone, and had a tendency to fall backward, but the voluntary power in the lower limbs was

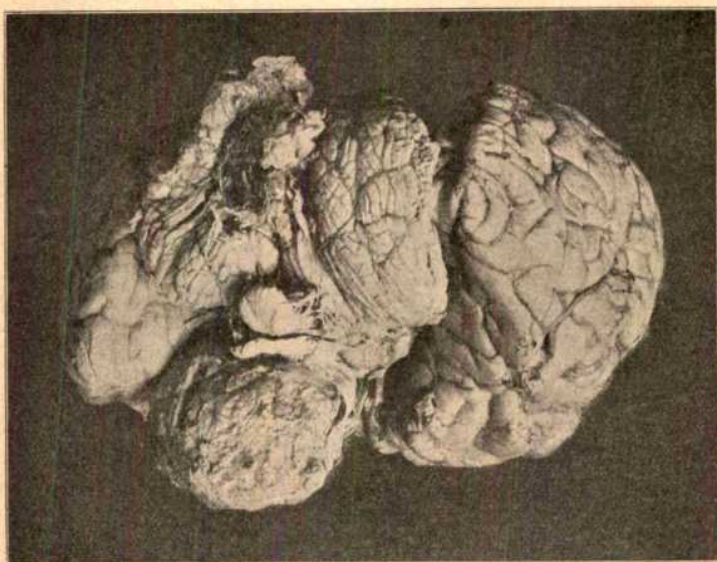


FIG. 5.

Case 5 [No. 296].—A tumour of the posterior cranial fossa. It has pushed the cerebellum between the occipital lobes as did the tumour in Case 1.

fair. She was very ataxic even in the heel-to-knee test. The patellar reflexes were exaggerated, and ankle-clonus and the upward movement of the toes in the Babinski test were obtained on each side. The movements of the upper limbs were ataxic, and the grip of each hand was weak. The biceps reflex was exaggerated on each side. The voice was whining. Weakness of the lower part of the right side of the face was present. The tongue deviated to the right when protruded. The right masseter muscle was weak, and the lower jaw deviated slightly to the right when the mouth was opened. These symptoms evidently were caused by pressure upon the left cerebral peduncle and left upper part of the pons. Reaction of the iris to light and in convergence was lost in each eye, and the left eye protruded. Swallowing was difficult. Mentality became much impaired, and stupor pronounced.

The body was in the cerebellar attitude described by Hughlings Jackson. Dr. Hansell found the late stage of high-grade optic neuritis passing into atrophy in both eyes. The left eyeball could be moved only slightly, and the movement preserved was downward, and slight ptosis was observed on the left side. Late in the disease the right eyeball deviated outward. The right upper limb was a little weaker than the left. Hunger was pronounced, and a second dinner was demanded nearly every day. The upper limbs became very rigid, the fingers were flexed into the palms and the forearms flexed on the arms across the chest. The lower limbs also became very rigid in extension and the feet over-extended.

A tumour measuring 9 cm. antero-posteriorly by 6 cm. laterally was found in the left cerebello-pontile angle. It was very nodular and well defined. It evidently had arisen from the dura at the base of the brain, and had affected the nerves coming from the left side of the medulla oblongata and pons by pressure only. The cerebellum had been greatly displaced laterally, but not so much as in Case 2, the edge of the right lateral lobe of the cerebellum not so nearly forming a right angle with the brain-stem. The tumour had forced apart the occipital lobes, and had depressed the basal part of the occipito-temporal lobe. It must have stretched the tentorium greatly. The greater part of the periphery of the tumour, especially the upper part, was covered by a dense fibrous membrane, and a piece of tentorium extended medianly from this membrane. The tumour pressed severely upon the left third nerve, but the right third nerve was not implicated. The posterior and anterior horns of the left lateral ventricle were much compressed. The right lateral ventricle was dilated at all parts. The tumour was a fibro-sarcoma.

Case 2 [laboratory number 558].—S. W., female, aged 33, was seen by me in consultation with Dr. H. D. Beyea, December 22, 1910. She had had severe headache for thirteen months. She had nausea and vomiting occasionally, and her condition had become much worse following an operation for retroflexion of the uterus three weeks previously. The pain in the head was almost unbearable and was of a burning character, and the head felt as though there were internal pressure. This pain was distinctly more intense on the left side, although it extended at times to the right side. Tinnitus like escaping air was heard in the right ear, and hearing was much impaired in the right ear; it appeared to be impaired also in the left ear. Pain had been felt frequently on the right side of the face. She had vertigo at times.

The patellar reflexes were exaggerated. She was ataxic on standing and walking, and the ataxia was increased by closing the eyes. Slight nystagmus was present in looking to the right.

Dr. B. A. Randall reported, December 23: "There is defect of hearing on the right side of moderate degree only for all tones, more marked for the weaker high or low tones. This corresponds with a lesion of the acoustic nerve, but in contradiction she claims transmission through the bone to the affected right ear."

Dr. Langdon, in Dr. de Schweinitz's clinic, on December 23, 1910, found

3 dioptries of swelling of the optic disc in each eye, and numerous hæmorrhages on and near the discs. On December 27 he found that the papillœdema had increased until the apex of each disc was $5\frac{1}{2}$ dioptries. In addition, several fresh hæmorrhages had formed.

The reflex of the right scleral conjunctiva and, to a less extent, of the right cornea was diminished. Diadokokinesis was good in each hand. Finger-to-nose test showed slight ataxia only on the right side. Asynergia was moderate; when the patient was told to bend the head and body backward she at first was not inclined to flex the knees, and nearly fell backward. When told to lift the upper part of the body, with the upper limbs folded across the chest, she was unable to do so at first, as she raised the lower limbs from the bed instead of pressing them against the mattress.

The most serious symptoms, therefore, were nausea, vertigo, headache (more on the left side), pain at times in the right side of the face, which was with difficulty to be distinguished from the headache, as it was not present at the time of examination; diminution of the right conjunctival and corneal reflexes; tinnitus and deafness, probably of nerve origin, in the right ear; rapidly developing papillœdema with numerous hæmorrhages; ataxia on standing and walking; exaggeration of the tendon reflexes of the lower limbs, that varied in intensity from one examination to another; ataxia in the finger-to-nose test and a moderate amount of asynergia.

My diagnosis was of tumour in the right cerebello-pontile angle, but as the deafness of the right ear was not positively of nerve origin, a tumour of the cerebellum could not be excluded. The right facial nerve showed no defect.

An opening of large size was made over the occipital region by Dr. C. H. Frazier, and the dura was slit. Much cerebrospinal fluid escaped. It was thought advisable to perform the operation in two stages, but the patient did not rally sufficiently to justify any further surgical procedure, and died within a few days.

A tumour, measuring 4 cm. antero-posteriorly by 2.5 cm. laterally, was found in the right cerebello-pontile angle. It was well defined, nodular, and at no part infiltrated the brain. It had displaced the cerebellum almost to a right angle with the brain-stem. The left lateral lobe of the cerebellum indented the pons. The right trigeminal nerve was attached to the tumour at its periphery, but was not involved within the tumour. A bundle of nerve-fibres, having the origin of the acoustic nerve, entered the tumour and was lost within it. It was impossible to determine without dissection whether this was the acoustic or facial nerve, or both, but no trace of any other nerve that could be either of these was found. The tumour pressed upon the right side of the medulla oblongata and flattened this side, and may have stretched the glosso-pharyngeal and vagal nerves. The pressure of the tumour upon the pons and medulla oblongata had not caused any distension of the lateral or of the third ventricle. The tumour was of the same character as that of Case 1, viz., a fibro-sarcoma. Mallory, however, regards these tumours as endotheliomata.

ON THE FUNCTION OF THE CHOROID GLANDS (CHOROID PLEXUSES) OF THE CEREBRAL VENTRICLES AND ITS RELATION TO THE TOXICITY OF CEREBROSPINAL FLUID.

BY S. P. KRAMER, M.D.

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SINCE the time of Luschka (1855) the choroid plexuses of the cerebral ventricles have been regarded as the secretory organs for the cerebrospinal fluid. These are highly vascular projections of the pia mater into the ventricles covered with villous-like processes about 1 to 2 mm. in diameter. Under the microscope these villi are seen to be made up of a number of secondary villi, which again show grape-like projections. Through the centre of the villi run comparatively thick-walled blood-vessels, giving the entire organ a highly vascular appear-

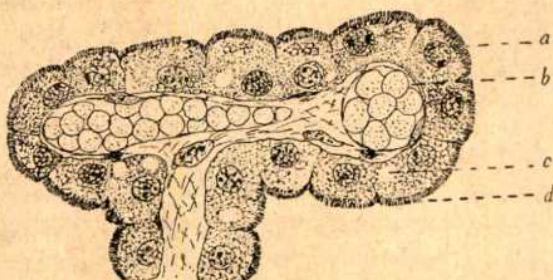


FIG. 1.

Cross-section of a portion of an adult rabbit's plexus. Magnification $\times 1,500$. *a*, microsomes simulating basal bodies; *b*, capillary with blood corpuscles; *c*, clear space (fat droplet); *d*, marginal zone. From Meek [1].

ance. Covering the villi is a layer of large spheroidal epithelial cells. The choroid epithelium is of the same embryological origin as the cells of the ependyma—*i.e.*, the inner layer of the neural tube. The epithelial covering consists of a single layer without intervening spaces. In some animals, and in man, many of the cells contain clear spaces which stain with fat-staining reagents; these are either fat or lipid bodies (fig. 1). According to Meek [1] these bodies or droplets increase in

size as they approach the apex of the cell and appear to be extruded without destroying the cells from which they come. Further, according to Meek, the cells from embryonic or young animals differ from those of the adult in that they are more columnar, less easily stained, and have the nuclei placed nearer the apex of the cell. This may be an indication of a change or awakening of function after birth. The connective tissue of the villi is that of the pia mater.

Benedict [2] described nerves in the choroid plexus of the fourth ventricle. Findlay [3] found nerve-fibres in the choroid plexuses of man accompanying the blood-vessels, possibly vasomotor in function. Petit and Girard [4], and later Meek, administered pilocarpine, muscarine and ether to animals, and examined the choroid cells to demonstrate changes due to secretory phenomena. Meek found that after the injection of muscarine in rabbits the height of the cells became doubled, the granulation at the base of the cells became heavier, and the apex clearer (fig. 2). Similar changes may be seen in the choroidal cells of



FIG. 2.

Three cells from an adult rabbit's plexus after injection of muscarine. Magnification $\times 1,500$. *a*, marginal zone which has become a thin granular line; *b*, clear spaces toward the apex; *c*, basal granular zone. From Meek [1].

a dog after the administration of ether. The whole appearance of these organs strongly suggests an inverted gland, which, instead of pouring its secretion into a series of ducts, empties directly into the ventricular system of the brain.

If the choroid plexuses are stripped from both the lateral ventricles of a dog recently killed by bleeding, and rubbed up in 2 c.c. of normal saline solution, the injection of the filtrate into the jugular vein of another dog will cause a marked fall in the blood-pressure. This effect was found to be constant in ten experiments. Fig. 3 is a tracing of such an experiment.

The blood-pressure was obtained by connecting the carotid artery of the animal with a mercury manometer. The time of injection was recorded by an electric signal. The injection was made into the jugular vein. The animals were under ether anæsthesia administered

through a tracheal tube. The animal received 1 c.c., or half the total extract made from the choroid plexuses of the lateral ventricles of another dog killed by bleeding without ether. The drop in blood-pressure which, in this experiment, began eleven seconds after the beginning of the injection, reached its maximum—*i.e.*, 50 mm.—thirty seconds after the beginning of the injection, and returned to the original pressure in two minutes. The rate of the heart-beat was apparently unchanged. Extracts made from the choroid plexus of the fourth ventricle produce the same reaction. Extracts made from the choroid plexuses of the human brain show the same effects in even smaller doses. Extracts made from the choroids of the rabbit, calf, and sheep do not show this



FIG. 8.

December 20, 1910. Dog, 10 kilos. Ether anaesthesia. Jugular injection of 1 c.c. extract of the choroid plexus of the lateral ventricle obtained from another dog killed by bleeding without ether.

Uppermost line—Seconds. Second line—Blood-pressure. Third line—Time of injection.

depressant reaction. The reaction is independent of the action of the vagus nerves, since the same effect is obtained when both vagus nerves have been divided. If the extract be heated to 60° C. for ten minutes its depressant power is lost. If the extract be thrown into a large quantity of a saturated solution of $MgSO_4$ the precipitate collected, washed with distilled water until free from magnesium sulphate, and then the precipitate be dissolved in a 2 per cent. sodium chloride solution and injected into the jugular vein of a dog, the same fall in blood-pressure is produced by the precipitate as was brought on by the original extract. From these facts, the conclusion has been reached that the "depressant" we are dealing with is a globulin. The thought suggested itself that possibly in certain cerebral affections, particularly in such as were associated with hyper-secretion of cerebrospinal fluid, this fluid might contain an excess of this "depressant" evidently secreted by the choroid plexuses. Accordingly, experiments were made with cerebrospinal fluid obtained by lumbar puncture in such cases.

Fig. 4 is a tracing obtained from a dog into whose jugular vein were injected 12 c.c. of cerebrospinal fluid obtained by lumbar puncture from a case of œdema of the brain following a blow to the head producing a sub-tentorial hæmorrhage. It will be seen that the injection caused a definite (55 mm.) and prolonged fall in blood-pressure, followed by an exceedingly slow and incomplete recovery. The cerebro-

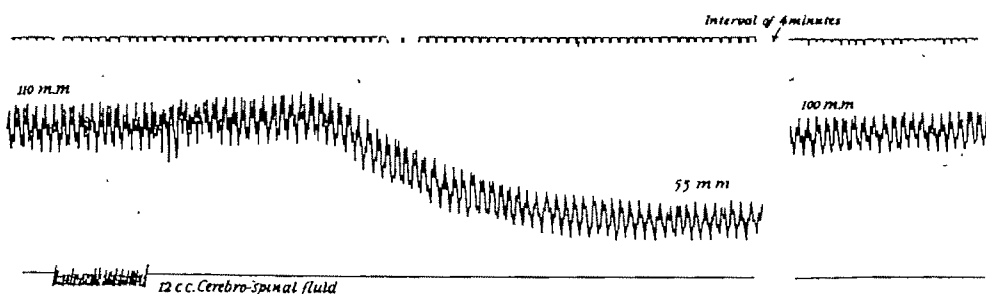


FIG. 4.

December 28, 1910. Dog, 12 kilos. Ether anæsthesia. Jugular injection of 12 c.c. cerebrospinal fluid from a patient with cerebral œdema of traumatic origin. Lines as before.

spinal fluid in this case evidently contained a great excess of the "choroid depressant."

Fig. 5 is a tracing obtained from a dog into whose jugular vein were injected 5 c.c. of cerebrospinal fluid drawn from a marked case of delirium tremens. This fluid was much more depressant than that from the previous case.

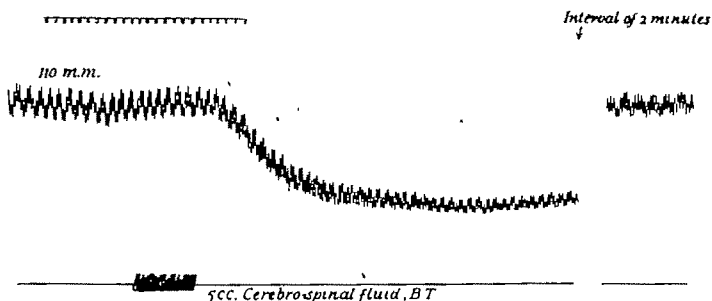


FIG. 5.

December 31, 1910. Dog, 6 kilos. Ether anæsthesia. Jugular injection of 5 c.c. cerebrospinal fluid from a fatal case of delirium tremens. Lines as before.

The injection of 10 c.c. of the same fluid fifteen minutes later into the same dog produced a most violent and prolonged depression, from which the animal incompletely recovered only after an interval of eight

minutes. In the case from which this fluid was obtained the individual died, and at autopsy great cerebral oedema was found. The ventricles were filled with fluid which, when injected into dogs, was definitely depressant. It is interesting to note that in a case in which recovery from delirium tremens occurred, the toxicity of the cerebrospinal fluid became much less.

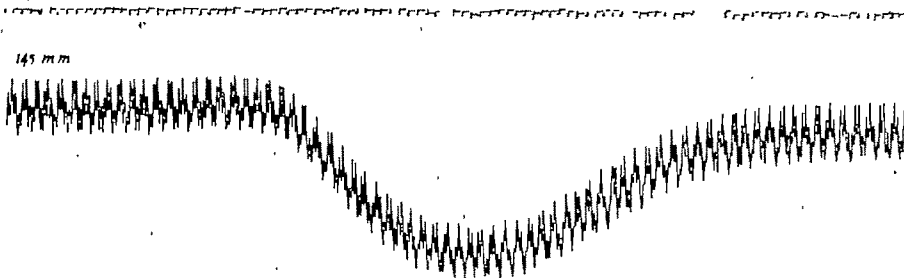


30 c.c. Cerebro-spinal fluid

FIG. 6.

January 3, 1911. Dog, 6 kilos. Ether anaesthesia. Jugular injection of 30 c.c. cerebrospinal fluid from an individual recovering from a mild attack of delirium tremens. Lines as before.

Fig. 6 is a tracing obtained by injecting 30 c.c. of cerebrospinal fluid drawn from a patient who had recovered from delirium tremens. There was but little depressant effect, a fall in blood-pressure of not more than 5 mm., which was quickly recovered. The individual from



15 c.c. Cerebro-spinal fluid Diabetic Coma

FIG. 7.

January 10, 1911. Dog, 8 kilos. Ether anaesthesia. Jugular injection of 15 c.c. of cerebrospinal fluid from a fatal case of diabetic coma. Lines as before.

whom the cerebrospinal fluid was obtained had had a mild attack of delirium tremens which had lasted only forty-eight hours, and at the time the fluid was withdrawn his pulse was normal and the delirium had disappeared. It should also be noted here that as the result of a

number of observations made in cases of delirium tremens, the removal of a quantity of cerebrospinal fluid appears to have an excellent therapeutic effect.

Fig. 7 is a tracing obtained from a dog into whose jugular vein were injected 15 c.c. of cerebrospinal fluid obtained in a fatal case of diabetic coma. The depressant effect is very distinct. At autopsy the lateral ventricles were found filled with fluid which was also extremely depressant.

A similar depressant result was obtained by Cushing and Goetch [6] as the first effect of injecting large quantities (50 to 150 c.c.) of cerebrospinal fluid concentrated on a water-bath, 80 to 1.

Dixon and Halliburton [5] found the intravenous injection of a saline extract of choroid plexus caused an increase in the secretion of cerebrospinal fluid, associated with a slight and temporary fall of blood-pressure. They found that boiling the extract did not destroy its action on the secretion of cerebrospinal fluid; and that the active principle was soluble in dilute and absolute alcohol. Their extracts were made from the choroid plexuses from the ox, sheep, and man.

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EPIDEMIOLOGY OF POLIOMYELITIS.

BY FREDERICK E. BATTEN, M.D.

INTRODUCTION.

THE purport of this paper is to collect and put together in a concise form the facts which are known in relation to poliomyelitis as an infective and epidemic disease. For this purpose the subject will be dealt with under the following heads:—

- (I) Definition of the term “poliomyelitis” and clinical aspect of the disease.
- (II) Nature of the virus.
- (III) History of past epidemics.
- (IV) Certain details in the investigation of some recent epidemics:—
 - (a) Wickman's investigation of Swedish epidemic, 1905.
 - (b) Lovell's investigation of Massachusetts epidemic, 1907.
 - (c) Krause's investigation of Westphalia epidemic, 1908.
 - (d) Lindner and Mally's investigation of Steyr epidemic, 1908.
 - (e) Potpeschnigg's investigation of Steiermark epidemic, 1909.
- (V) Epidemics of poliomyelitis in Great Britain in 1908, 1909, 1910.
- (VI) Distribution of the disease in London in 1904.
- (VII) Conclusion.
- (VIII) Appendix, list of epidemics, literature.

(I) DEFINITION OF THE TERM “POLIOMYELITIS” AND CLINICAL ASPECTS OF THE DISEASE.

THE term “poliomyelitis” has been used to designate the disease under discussion because it is a name that has come into general use, and calls up to most people the clinical picture of a child with a flaccid palsy of one or more limbs. Personally, I prefer the term “polio-encephalomyelitis,” indicating that not only the spinal cord but any part of the nervous system may be affected. The term “infantile paralysis” is objected to because, although children are to the largest extent affected, yet the disease is by no means limited to them.

The terms "Heine-Medinsche Krankheit" and "epidemic paralysis" have been suggested. With regard to the first, it has the objection common to all diseases described by men's names—viz., that the name conveys no indication of the nature of the disease. With regard to the second, I think there is much to be said in its favour; paralysis is a wide term and would include most of the manifestations of the disease, the word epidemic, although true with regard to a large number of the cases which occur, yet is by no means always so.

It is important to have a clear understanding of the clinical aspect of this disease. Poliomyelitis or polio encephalomyelitis is an acute infective disease, having a special selective action on the nervous system, and giving rise to a variety of symptoms dependent on the portion of the nervous system affected. Such symptoms may be (1) a localized paralysis of one or more limbs; (2) an ascending paralysis, often rapidly fatal owing to the involvement of the respiratory centres; (3) an acute ataxia; (4) a paralysis of one or more cranial nerves; (5) hemiplegia; (6) the symptoms of meningitis; (7) an acute mental defect; and (8) a type of case in which pain, especially on movement, is the most marked feature—so-called neuritis.

Such is the modern conception of the disease. It is fully recognized that there are abortive cases with transient symptoms with or without paralysis; but these cannot be identified except when occurring in direct association with a marked case of the disease. Their true nature will only be fully proved when some serum reaction or animal test is forthcoming.

(II) NATURE OF THE VIRUS.

It is not the purpose of this paper to deal with the nature of the virus of poliomyelitis, but no paper on the epidemiology of the disease can be complete without a clear understanding as to what is known of the virus. The work of Landsteiner, Popper, Levaditi, Flexner, and Lewis has shown that the disease is transmissible from man to monkeys by inoculation, that it is transmissible from monkey to monkey, that the virus is not killed by glycerination, and that it will pass the finest filter. The organism has not yet certainly been cultivated *in vitro*, has not yet been stained, and has not been seen under the highest powers of the microscope. The virus can be obtained from the mucous membrane of the nose of a monkey which has suffered from the disease, and may be obtained from this situation

six months after the date of the infection in a still active condition (Osgood and Lucas).

The virus is killed by an exposure to a temperature of 55° C. for half an hour, it is not killed by an exposure to a temperature of -8° C. The virus is not eliminated by the saliva, the urine, or the fæces.

Monkeys living in the same cage with infected monkeys fail to contract the disease. This is attributed to the intact condition of the mucous membrane, for it is only possible to infect an animal by way of the mucous membrane after injury to this membrane. There is some evidence to show that there are slight differences between the virus of Flexner and that of Landsteiner.

Levaditi states that the virus of Flexner is neutralized *in vitro* by the serum from a monkey which has been rendered immune to the Flexner virus. It is not neutralized by the serum of a monkey rendered immune to the Landsteiner virus. On the other hand, the virus of Landsteiner is neutralized by the serum of a monkey rendered immune to the Landsteiner virus, but it is not neutralized by the serum from a monkey rendered immune to the Flexner virus.

The Flexner virus is more virulent than the Landsteiner virus. The result of these researches would seem to indicate that there is a variation in the virus similar to that seen in the typhoid and paratyphoid organism.

It has been shown by Landsteiner and Levaditi that when the virus is introduced into a nerve-trunk the virus probably travels by the lymphatic spaces of the nerves and reaches the spinal segments at the entrance of the nerve-roots, so that the paralytic phenomenon always occurs in the limb corresponding to the nerve-trunk inoculated.

Further, it has been shown by Leiner and Wiesner that after the virus has been introduced into the peripheral nerve, the infection of the animal can be prevented by section of the nerve above the point of inoculation.

Animals other than the monkey and ape seem to be immune, although Meinicke states he is able to infect rabbits. The similarity of the virus with that of rabies is striking. The pathological lesion in poliomyelitis is also very similar to that of rabies. It has recently been stated by Vipond that cases of poliomyelitis give a positive Widal reaction. In no case which has been tested for me by Dr. Forbes, Pathologist to the Children's Hospital, has a positive Widal reaction been obtained, neither has he succeeded in finding the organism described by Dixon, Fox, and Rucker in the blood of cases of poliomyelitis, but the number of such cases is at present too small to be of any great value.

up till 1907 will be found in the paper by Holt and Bartlett, and further details in the papers of Wickman and Job and Froment.

Since 1907 I have collected the record of some 26 epidemics in all parts of the world, and these, together with those previous to 1907, are recorded in a list which is appended to this paper.

The leading features of the past epidemics may, however, be shortly stated. The first record of the disease in an epidemic form comes from Sweden in 1881. (I have purposely omitted an epidemic

EPIDEMIC POLIOMYELITIS.

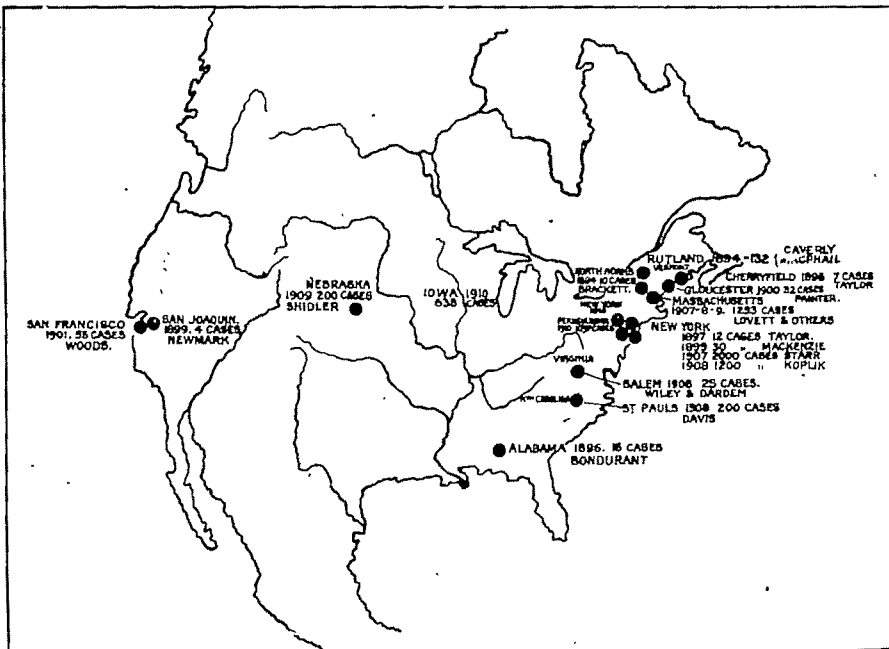


FIG. 2.

Map of America, showing the places at which epidemics of poliomyelitis have occurred, the number of cases in the epidemic, the date of the epidemic, and the name of the recorder.

recorded by Colmer in America in 1841, because I can find no account of it.) In 1883 some groups of cases were recorded in Italy, and in 1886 in Norway, Germany, and France. All of these epidemics were small in numbers. In 1887, however, Medin described an epidemic in Stockholm of 44 cases, and this is the first important work on the subject. In 1894 an epidemic occurred in Rutland, Massachusetts, of 132 cases, which was recorded by Caverly and McPhail. Small epidemics were recorded in the 'nineties in Italy, France,

Australia, England and America, and a larger epidemic of 42 cases occurred in Vienna in 1898, and in Norway in 1899, and in Sweden in 1899. The latter epidemic was recorded by Wickman, to whom so much is due with regard to the investigation of the pathology and the spread of the disease. In the middle of the next decade, viz., 1900 to 1910, the record of cases, which before had been limited to two figures, now reached to four figures, and during the years 1903-07 it may be said that the disease was pandemic in Norway and Sweden, and during the years 1907-10 large epidemics occurred in the State of New York and in the State of Massachusetts. At the same time epidemics of the disease were recorded in Australia (Stephens), in Vienna (Zappert), Westphalia (Krause and Reckzeh), in Paris (Netter), in Austria (Fürntratt, Potpeschnigg, Lindner and Mally), Switzerland (Hagenbach), in Russia (Jogichess). (See maps, figs. 1, 2, 3.)

EPIDEMIC POLIOMYELITIS.

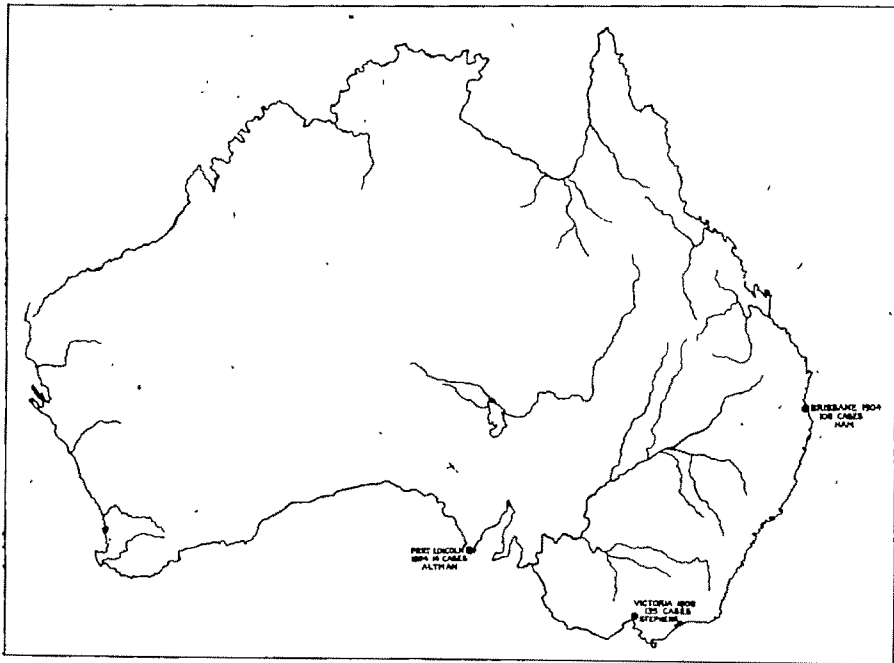


FIG. 8.

Map of Australia, showing the places at which epidemics of poliomyelitis have occurred, the number of cases in the epidemic, the date of the epidemic, and the name of the recorder.

During the year 1910 the number of cases of poliomyelitis, and deaths caused by the disease, recorded in the United States is as

follows: Pennsylvania heads the list both in prevalence and in mortality; there were 1,097 cases and 172 deaths in that State. In Iowa there were 638 cases and 161 deaths. In Massachusetts there were 588 cases; the number of deaths is not given. Apparently the epidemic was most continuous in Iowa, for that is the only State from which cases and deaths were reported for every month of the year. The maximum number of cases in any month was 378 in September in Pennsylvania; the maximum number of deaths, 64, in the same month and the same State. The maximum number of cases in any month in the entire Union was 1,146, in September; the maximum number of deaths, 182, in August. The total number of cases and deaths of poliomyelitis in the United States during the year 1910 was 5,093 and 825 respectively, a mortality of about 13.75 per cent.

I have made no attempt to give all the rest of the epidemics, and for these I must refer the reader to the list in the appendix, but I have said enough to show that epidemics were widely distributed over the whole of Europe, and were present in America and Australia. Though I can find no record of South Africa having suffered, yet I know from private information that the disease was epidemic in Pietermaritzburg in 1902, and I have seen other cases which have occurred in South Africa during the past ten years.

(IV) CERTAIN DETAILS IN THE INVESTIGATION OF SOME RECENT EPIDEMICS.

Most epidemics have their particular interest, and it is sometimes from the investigation of small epidemics that most is to be learnt. In the present instance, however, the evidence is so largely on the negative side that I have selected a few of the best investigated recent epidemics as instances of what has been done. I propose to select the following for consideration: Wickman's investigation of the Swedish epidemic of 1905; Lovell's Massachusetts epidemic, 1907, 1908, 1909; Krause's Westphalian epidemic, 1908; Lindner and Mally's Steyr epidemic, 1908; and Potpeschnigg's Steiermark epidemic, 1909.

Factors common to all Epidemics.

There are certain factors common to all epidemics, and these may be shortly stated.

Seasonal relationship.—In the Northern Hemisphere the disease always has the greatest prevalence during the months of July, August,

September and October, the month of August being nearly always that in which the greatest number of cases occur. In the Southern Hemisphere the disease has occurred during the months of March and April—i.e., months which, I believe, in atmospheric conditions correspond fairly well to September and October in the Northern Hemisphere.

Age incidence.—The incidence of the disease on young children is a constant feature, and it commonly falls upon children during the second and third years of life. Babies in arms are rarely affected; as the age advances the incidence rapidly declines. In the Massachusetts epidemic, of 440 cases under 6 years of age, 304 occurred in children between 1 year and 4 years old.

The mortality.—The mortality in the various epidemics varies considerably; over the total number of cases it amounts to from 11 per cent. to 12 per cent. One epidemic had a mortality of 18 per cent. (Rechzeh), and another had a mortality of 5 per cent. to 6 per cent. A great deal depends on how these statistics are made up and whether the abortive cases are included. The mortality is higher for children of older age than it is for young children. In the Massachusetts epidemic the total death-rate was 8 per cent., whereas the mortality in children over 10 years of age was 20 per cent., for under 1 year of age 16 per cent., and between the ages of 1 and 10, 4 per cent.

(a) *The Swedish Epidemic of 1905 (Wickman).*

In this epidemic the incubation period was shown to lie between one and four days, 74 of the 127 cases coming within this period. There are some striking individual cases of isolated contact which show that the incubation may be as short as twelve hours. As a good instance of school infection one may take the outbreak that occurred in the parish of Trästena.

The first cases occurred in Sandbäcken, a neighbouring village, in February and March; three children were affected and one died. An interval of three months now elapsed in which there were no cases. At end of May and beginning of June, two cases occurred in the same house in Marienstad, a village a mile off. There was then another interval till the end of June and then the outbreak at Trästena began. The first case occurred on June 28 in an isolated house. Early in July a series of cases occurred, mostly in connexion with the school. In this village, out of 102 houses 19 were affected. The numbers of the individuals affected in each house were as follows: In six houses, one

case; in three houses, two cases; in five houses, three cases; in three houses, four cases; in two houses, five cases. (See fig. 4.)

The school was infected on June 28, and a series of cases occurred on July 3, 4, 8, 10, and 12. The school was shut on July 15. Other cases occurred during the month, and the last on August 4.

In this little parish of Trästena, with 500 inhabitants, 49 persons were affected, 23 with the abortive form of the disease, 26 with the paralytic form. Of the cases with paralysis; 11 died—i.e., 42.3 per cent.

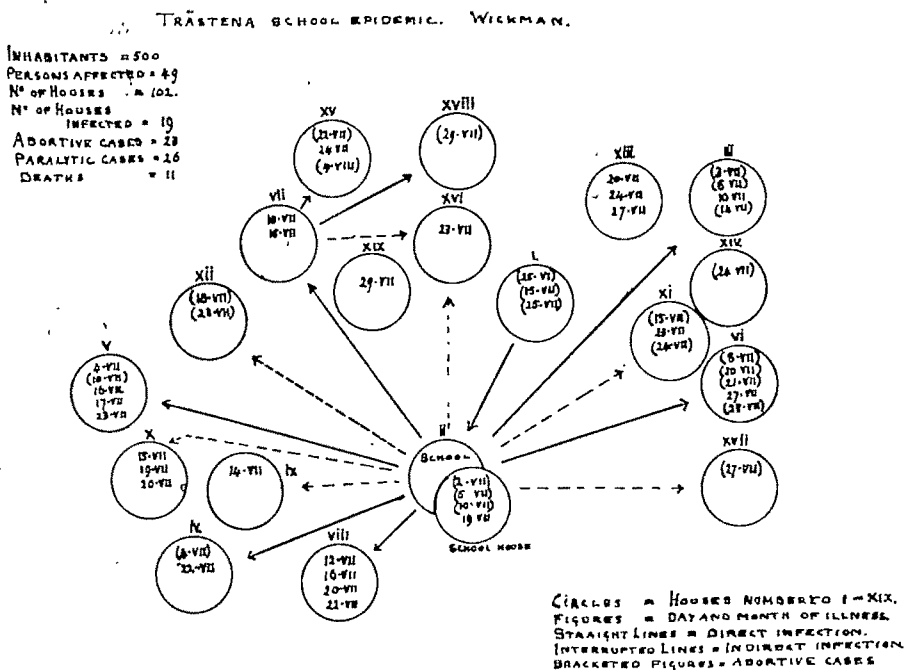


FIG. 4.

Three other instances of a school being a source of infection are given by Wickman. The disease appears always to be carried by contact, but the contact may be by means of a perfectly sound and healthy individual. The disease was most prevalent in Sweden in 1905 and was less in 1906 and 1907.

(b) *The Massachusetts Epidemic.*

Epidemics of poliomyelitis have been investigated in Massachusetts in the years 1907; 1908, 1909. In the year 1907 some 234 cases were

recorded; in the year 1908, 136; and in the year 1909, 923. Most of the cases occurred in and around Boston. The transmissibility of poliomyelitis is shown to be considerably less than either scarlet fever or diphtheria. Of persons known to have been exposed to diphtheria, scarlet fever, and poliomyelitis, the percentages of those infected were as follows: Scarlet fever, 22 per cent.; diphtheria, 17 per cent.; poliomyelitis, 6 per cent. The investigators dealt with 150 of the cases of the 1909 epidemic in detail.

Rainfall, temperature, surroundings, nearness to railroad, nearness to water, age of house, sanitary conditions, location of house, character of house, floor of house inhabited by a family, sewage disposal, character of water supply, relation to dust, prevalence of vermin, insects and rodents, data as to domestic animals kept, occurrence of paralysis in animals, swimming and wading, exposure to heat, cold or damp, diet, and attendance at school, were all investigated. I do not propose to give the results of the investigation of all these various points; most of them are strikingly negative. One or two, however, deserve some mention. Of the 150 cases, 62 were swimming or wading in water more or less contaminated by sewage before the attack. In 87 of 142 families affected, animals of some sort were kept, and in 34 of these there was some illness or paralysis. In no case was a child living on breast milk alone affected by the disease. Thirty-five of 150 cases attended school: the school could *not* be shown to be a source of infection. Another most interesting point is that only one child out of 3,600 who lived in forty-five institutions was affected with the disease. With regard to animal infection the following note from Dr. C. S. Shore is of interest:—

“In my veterinary practice during the past five or six years, I have found a disease appearing among one- and two-year-old colts that shows a line of symptoms corresponding very closely to anterior poliomyelitis of children. I have had from five to ten cases a year during this time, the cases always occurring during the summer months, and the majority of them during the month of August. The affected colts are usually found in the pasture, unable to stand. The owner sometimes will notice an unsteady gait for twenty-four hours before entire loss of motion occurs. At first these colts have a rise of temperature ranging from 103° F. to 104° F.; pulse and respiration accelerated; animal sweats profusely; appetite remains fairly good, but there is some trouble noticed in swallowing, especially water; slight derangement of the bowels, tending toward constipation; more or less tympanitis present; retention of urine, for a few hours at least; head drawn back so that the end of the nose tends to assume a position somewhat on a line with the neck. The death loss

is less than 10 per cent., but in those that do not recover the market value is depreciated to a very great extent because of the faulty gait the animal assumes after an attack of this disease, due to atrophy and contraction of certain muscles, or certain groups of muscles. It seems that the flexor muscles of the limbs especially are more often affected than the extensor, and in almost all the cases some of these deformities are likely to remain permanent. The flexors of the limbs are liable to contract and cause volar flexion of the fetlock. The elevators of the head are also likely to become affected, so as to cause the head to have a poky appearance—that is, it is carried out from the body. After one of these attacks the colt will remain down from one to three weeks, and will then continue to improve for a period of one year, but seldom, if ever, makes a complete recovery.—Dr. C. S. SHORE, Lake City, Minnesota."

I have referred this question to Sir John McFadyean, and he states that he has never seen such a disease in young colts.

(c) *The Westphalian Epidemic of 1908 (Krause).*

In this epidemic, which occurred in and around Hagen in June, July, August, September, and October, 1908, there were 634 cases with 66

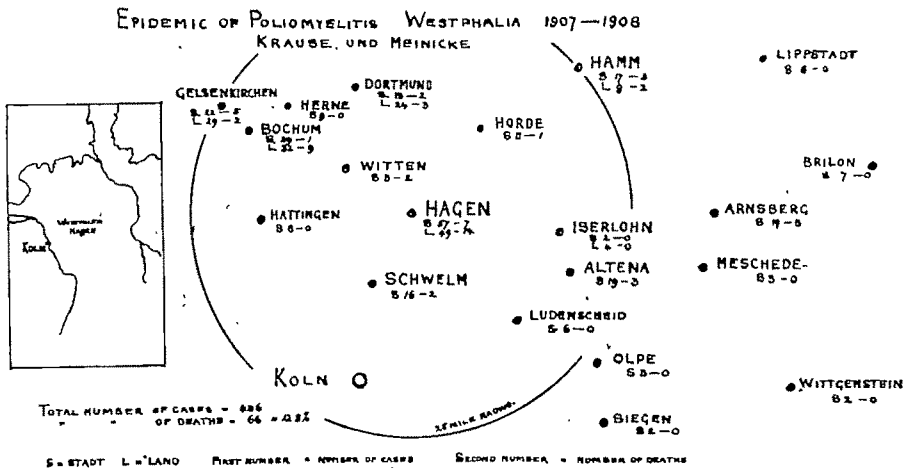


FIG. 5.

deaths. The epidemic is not worked out carefully from the point of view of its spread from town to town. Individual instances are given of the carriage of the infection from person to person. A grandmother is said to have carried the disease from one grandchild to another who lived in a different town. A mother infected her own child after visiting her infected nephew, and in two instances members of the same family were simultaneously affected. An instance is given in which, at the same

time that the daughter of a family was taken ill, two young hens died with paralytic symptoms. The examination of these animals gave a negative result. Krause says the disease not infrequently occurs in children at the breast. He believes that the entrance of the virus is by the intestinal tract, since 90 per cent. of the cases had intestinal symptoms (*see fig. 5*).

(d) *The Steyr Epidemic.*

In the epidemic which occurred in Steyr in the late summer of 1908, described by Lindner and Mally, 92 cases are described; 16 of these died. Of these

1 case occurred in 34 houses	4 cases occurred in 1 house
2 cases " 16 "	6 " " 2 houses
8 " " 1 house	7 " " 1 house

Two points especially attract attention, the first is the short period between the infection of members of the same family, and the second is the way the disease distributed itself along the railway line and the valley running out of the main valley in which the rail runs. The conclusion arrived at is that the infection of poliomyelitis is carried from individual to individual, and not by means of water or food material, and that the school is a method of disseminating the disease.

(e) *The Steiermark Epidemic, 1909 (Potpeschnigg).*

This epidemic began in September, 1909, and amounted to 434 cases, 60 of which occurred in Graz, and there was a mortality of 13 per cent. The question of the contagiousness of the disease was discussed. In favour of such a view is the fact that more than one member of the family may be affected, and also that persons coming in contact with the infected develop the disease. As an instance of this the following case is given: At the end of June the two-year-old child of a tailoress was taken ill with meningeal symptoms, and died in a few days of the "Heine-Medin" disease. To this child, when ill, the two-year-old child M. K. was brought to play, and sat on the bed. Six to eight days later the child developed typical poliomyelitis, there being no other possible contact. In Leibnitz, a place in Mid-Steiermark, the seven-year-old school child M. P. was taken ill on June 20; two days later the six-year-old child A. S., who sat next to her at school and was her playfellow, had follicular tonsillitis. In the course of the week the mother of this child and five brothers and sisters had tonsillitis, and of these the mother and two children had poliomyelitis.

Against the infectivity of the disease may be urged, *first*, the absence of spread of infection in hospital. The cases of poliomyelitis admitted to hospital freely mixed with other cases in the ward without any isolation or disinfection, some 70 children came in contact, but no infection took place. On these grounds it is probable that the paralytic stage of the disease is not contagious. *Secondly*, the striking absence of infection when contact has been most close. In November, 1909, H. E. was taken ill with poliomyelitis; all five brothers and sisters, although in closest contact, remained unaffected. In October, 1909, M. K., aged $2\frac{1}{2}$, was taken ill; two sisters, aged 6 and 11 respectively, slept with and were in close contact with the child and remained unaffected. Twin sisters, aged $2\frac{1}{2}$, one was affected, the other unaffected. *Thirdly*, that contact is not the only possible method of dissemination of poliomyelitis is proved by the fact that the disease may arise in persons in whom all contact with affected persons can be excluded.

The instances given of this are as follows: In 1908 the child of a cowkeeper, 30 kilometres removed from the next place in the Alps, was taken ill with poliomyelitis. The child of a railway watchman, whose house could only be reached through a long tunnel, was affected. The contact in school to which Wickman attaches so much importance could not be shown to be a factor in the Steiermark epidemic. It is striking that a large percentage of children are affected before the school age—viz., between 1 and 5 years.

(V) POLIOMYELITIS AS AN EPIDEMIC DISEASE IN GREAT BRITAIN.

So far as I know, there is no record of any epidemic of poliomyelitis in England before 1897, when W. Pasteur described the affection in seven members of one family. That record has become historic, as it is the record number of members affected in the same family.

Thomas Buzzard, in 1898, published a lecture "On Cases illustrating the Infective Origin of Infantile Paralysis." He gives an instance of two sisters residing in the same house who were attacked with paralysis within six days of each other. Four other children of the same family escaped. Two other children living in a neighbouring street were taken ill in a similar way in the same week. Buzzard also mentions a case in which a man cut his knee and stopped the bleeding by using moss from the roadside. A week later he was affected with poliomyelitis. He also mentions a case, seen in 1895, of a brother and sister who were taken ill within two days of one another; the sister was feverish and recovered without paralytic symptoms, the brother

was paralysed in the left arm. These two cases are alluded to in Buzzard's presidential address before the Clinical Society in 1895.

It has, of course, long been recognized that poliomyelitis is prevalent during the summer months in London, and especially during August and September. I have recorded an undue prevalence in 1902.

Upminster Epidemic, 1908.

In 1908 Treves reported an epidemic of eight cases in July, August, and September, 1908, at Upminster, a small village in Essex on the London, Tilbury, and Southend Railway, with a population of 1,477.

	No.	Name	Age	Taken ill
	1	Gertrude H.	3½	July 27; paralysis August 3
	2	John C.	13	August 24; paralysis August 27
Return from Westgate August 18 (sisters)	3	Enid H.	11	August 24; paralysis August 30
	4	Maud H.	12	August 24; not paralysed
Return to Upminster, September 3 (brother and sisters)	5	Stanley M.	8	September 9; paralysis Sep- tember 11
	6	Eva M.	10	September 11; paralysis Sep- tember 13
	7	Gladys M.	6	September 12; paralysis Sep- tember 14
	8	Basil J.	13	September 16; paralysis Sep- tember 16

With regard to incubation period, the child in whom the disease first started had not been out of Upminster, so the disease must have originated in that village. E. and M. H. returned to Upminster on August 18, and were attacked on August 24. The M. family returned to Upminster on September 3, and the first was taken ill on September 9, so the incubation period could not have exceeded six days.

Bristol Epidemic, 1909.

An epidemic of 37 cases is reported by George Parker in Bristol during the year 1909. Thirty-two of these occurred between June and October—i.e., during the summer (a cold and wet summer). The ages of the patients varied from 4 months to 16½ years. Three were adolescents. The average age of the children was 2 years. There was only one family of eight children in which two members were found to be affected. Two pairs of cases lived within a few doors of one another, but the interval between their attacks was, in one instance, July and November, and in the other, September and December. This epidemic was investigated after its occurrence, and probably only represents the most severely affected individuals of a hospital class. Two patients died, giving a mortality of 5 per cent.

EPIDEMIC POLIOMYELITIS.

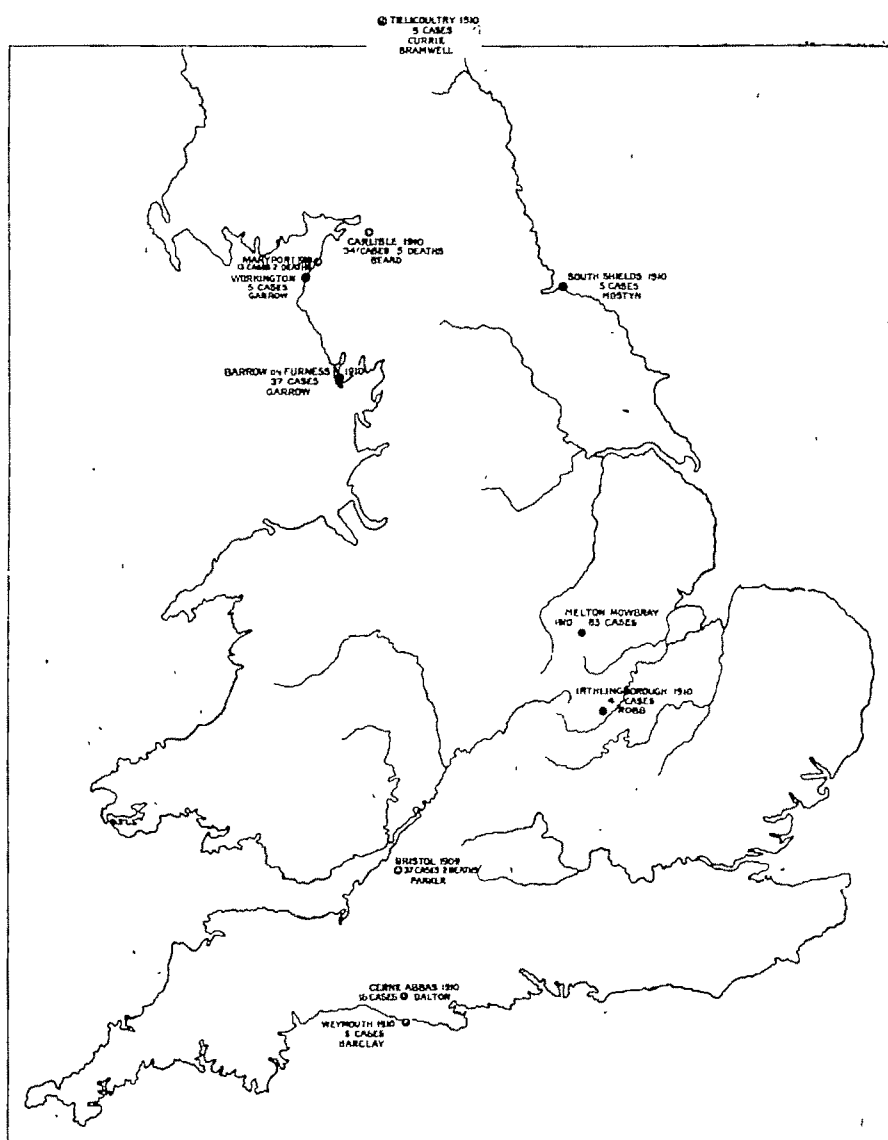


FIG. 6.

Map of England, showing the places at which epidemics of poliomyelitis have occurred during 1909-10, the number of cases in the epidemics, the date of the epidemic, and the name of the recorder.

Epidemics in England, 1910.

Garrow reported 13 cases of poliomyelitis in the town of Maryport, Cumberland, in August and September, 1910. One of these cases occurred at the village of Crosby, a little way out of Maryport—this child, aged 1 year and 10 months, died. It is worthy of note that her elder sister suffered from an attack of poliomyelitis on June 16, 1908, when 2 years and 3 months old, and recovered almost completely in four months.

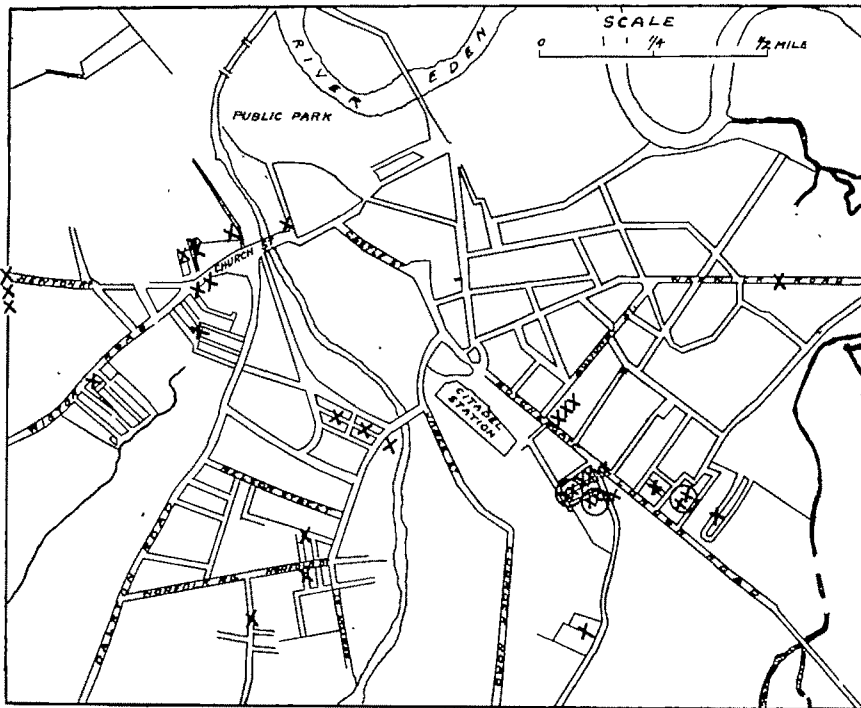


FIG. 7.

Street plan of Carlisle. The X's indicate the cases of poliomyelitis occurring during September, 1910. There were thirty-four cases, of whom five died. There were three instances of two members of one household being affected. These are marked with a circle on the map. Reported by Dr. Beard.

Dr. Garrow has been most kind in furnishing me with further information which he has collected about the epidemics of Workington and Barrow-in-Furness, and Dr. Beard, the Medical Officer of Health, has furnished me with the following details of the epidemic in Carlisle in September, 1910. He, recognizing that the disease was occurring in

an epidemic form, obtained the sanction of the Health Committee to make the disease notifiable. In Carlisle 34 cases were notified; five died. Of the remaining 29, one only appears not to have had the disease. Of the 28 cases, 12 will probably be incapacitated for the

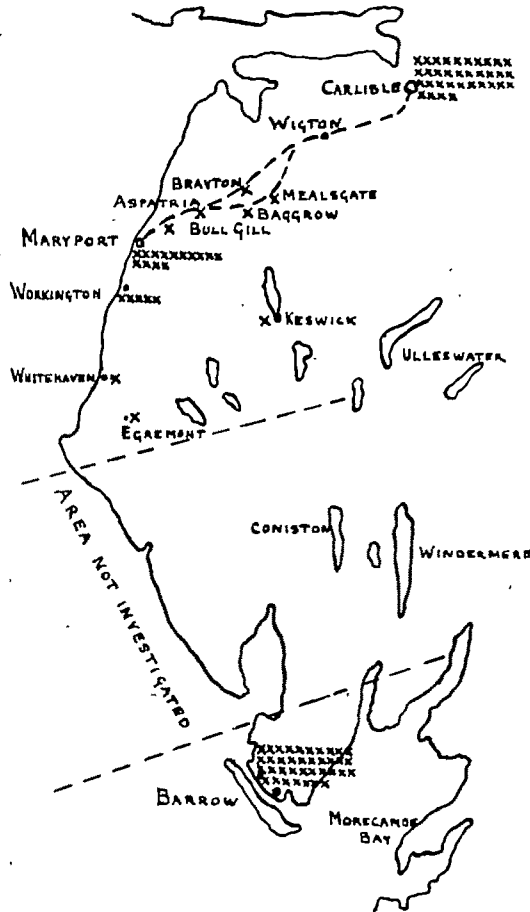


FIG. 8.

Coast of Cumberland, investigated by Dr. Garrow. The X's indicate the cases of poliomyelitis which occurred in 1910. Epidemics occurred in Carlisle, Maryport, Barrow-in-Furness, and other places.

remainder of life, either from total or partial paraplegia, hemiplegia, or monoplegia of leg and arm. In Carlisle there are three examples of two cases occurring in the same houses, all three examples being in that part of the town where the cases were most common; the pairs of cases are enclosed in a circle on the map (*see* fig. 7).

Dr. Garrow investigated the West of Cumberland and came upon scattered instances of the disease at various villages, as indicated on the chart (see fig. 8). At Barrow-in-Furness he found about 37 cases of permanent cripples. As he says, one can only guess at the actual number of cases. The severe cases which died and the slight cases

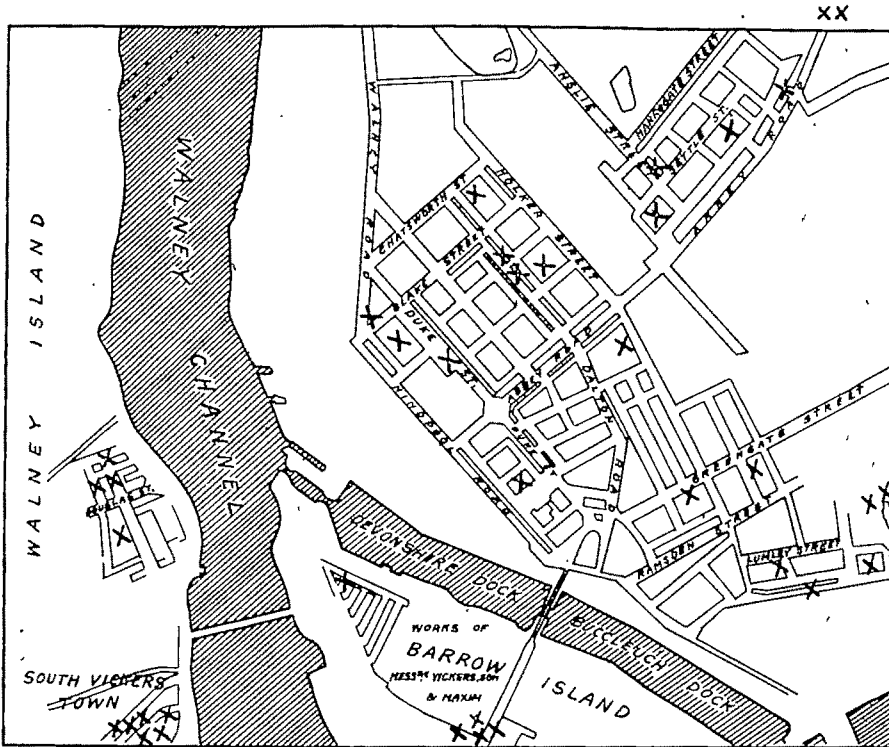


FIG. 9.

Street plan of Barrow-in-Furness. The X's indicate the cases of poliomyelitis occurring during 1910. There were thirty-seven cases. Map prepared by Dr. Garrow.

which recovered are lost for statistical purposes. The incidence of the disease seems to have fallen heavily on North and South Vickers Town: four cases in the former, six in the latter. Dr. Garrow says these are recently built model villages, situated on the slopes of Walney Island, about 50 ft. above sea-level. The houses are well built, streets well paved and clean, and the sanitation modern. The houses have good water supply, and are lighted by electric light. In short, the hygienic conditions are well-nigh perfect (see map, fig. 9).

With regard to the epidemic in the Midlands, which occurred around Melton Mowbray, I can furnish no detailed information, as the matter is under investigation by the Medical Officer of the Local Government Board, and his report is not yet published. It is known, however, that 83 cases occurred, with 14 deaths—i.e., 16·8 per cent. The epidemic was at first reported as one of cerebrospinal meningitis, but probably because observers did not recognize the meningeal form of poliomyelitis.

Dr. Robb, of Irthlingborough, Northamptonshire, reported a small epidemic of four cases occurring within a radius of 200 yards, and as far as he could gather there was no intercommunication between the respective houses. The cases were as follows:—

Case I.—E. M., aged 2½ years, was taken ill at the end of August, 1910, with feverishness and fretfulness, which the mother put down to teething; paralysis of the left leg was noticed next morning.

Case II.—J. H., aged 2, taken ill at end of August, 1910; paralysis of left leg and arm.

Case III.—W. M., aged 3, taken ill first week in September, 1910; paralysis of the left leg.

Case IV.—T. H., taken ill end of September, 1910; paralysis of left arm and leg. He quite recovered by Christmas.

Dr. Robb says: "Although I have been in active practice for over twenty years I have not, to the best of my recollection, had a series of such cases within so short a time."

Dr. Dalton, of Cerne Abbas, reported another small epidemic of 16 cases which occurred in Cerne Abbas, in Dorsetshire. The first of these cases occurred on September 29 and the last on October 24, 1910. Fourteen of these cases were in children under 8 years of age, one case in a boy 14 years old, and one in an adult 36 years old. There were two deaths—in children aged 14 years and 6 years respectively. Four remained badly paralysed, the others made good recoveries. Except for one case in an isolated cottage on the hills the disease was limited entirely to the parishes of Cerne Abbas and Upper Cerne. The former has a population of about 600; the latter, a mile away, is just a small village. In one house Dr. Dalton reports three cases out of four children; in another, two out of three; in another, one out of six; in another, one out of three; in another, one out of four; in another, two out of three. The adult case, a man, the father of four children, lived in quite a small cottage. It seemed almost impossible for the children to escape infection, and yet they did. The possible source of infection in this case was that the man was clipping a horse in a stable with the father of a child

suffering with the disease. No local condition could account for the disease, and many cases were in the better houses. The cases were quite scattered as regards houses. Isolation and disinfection of contacts and possible carriers seemed at once to stop further spread of the disease. Dr. Dalton suggests that foreign flour is the carrier of the disease.

In relation to the above epidemic Dr. W. B. Barclay, Medical Officer of Health for Weymouth, says there were five cases of poliomyelitis and one death during the year, and that he knew of none in the previous six years.

There appears to be some evidence that the disease was prevalent in and about Newcastle, but the facts obtainable are scanty and may possibly represent simply the normal incidence of the disease. Five cases were mentioned to Dr. Mostyn, the Medical Officer of Health for South Shields. A series of cases occurred in and about Hexham, and the Medical Officers of Health, Dr. Penford and Dr. Jackson, both consider that the cases have been more frequent than formerly.

In York two deaths were registered from the disease, and in Gloucester Dr. Bond reports three cases in one family.

The evidence obtainable from the Medical Officers of Health must of necessity be most defective in regard to a disease which does not come within their province; but I would wish here to thank all the Medical Officers of Health who have so kindly and courteously answered the questions and returned the post-cards sent to them.

One other small epidemic in September, 1910, is reported by Currie and Bramwell. It is known as the Harvieston epidemic, a private estate near Tillicoultry, in Clackmannanshire. The farmstead consists of four houses, which may be designated A., B., C., D. House A. is occupied by the factor, the three adjacent cottages by farm employees and their families.

The A. family consists of 2 children, A.A., aged 5; B.A., aged 2½.
 „ B. „ „ 4 „ A.B., aged 7½; B.B., aged 5½; C.B., aged 4;
 „ „ „ „ D.B., aged 7½.
 „ C. „ „ 4 „ All aged over 8.
 „ D. „ „ 2 „ Aged 2, and a few months respectively.

Five children in these four houses were attacked, A.A., B.A., A.B., B.B., and D.B. Children taken ill in following order:—

B.B.	...	September 12	...	Returned to school September 26.
A.B.	...	September 16	...	Paralysed on September 19.
D.B.	...	September 18	...	Squint.
B.A.	...	September 20	...	Paralysed right face.
A.A.	...	September 24	...	Paralysed both lower limbs.

From a consideration of the facts relative to these cases, the authors came to the conclusion that the incubation period in this epidemic was four days, or less, and from the fact that the children of the A. family did not visit the children of the B. family after the first child, B.B., was taken ill, but that the mother of the A. family visited and nursed the B. children whilst ill, the infection to the A. family was probably carried by her.

(VI) DISTRIBUTION OF CASES IN LONDON, 1904.

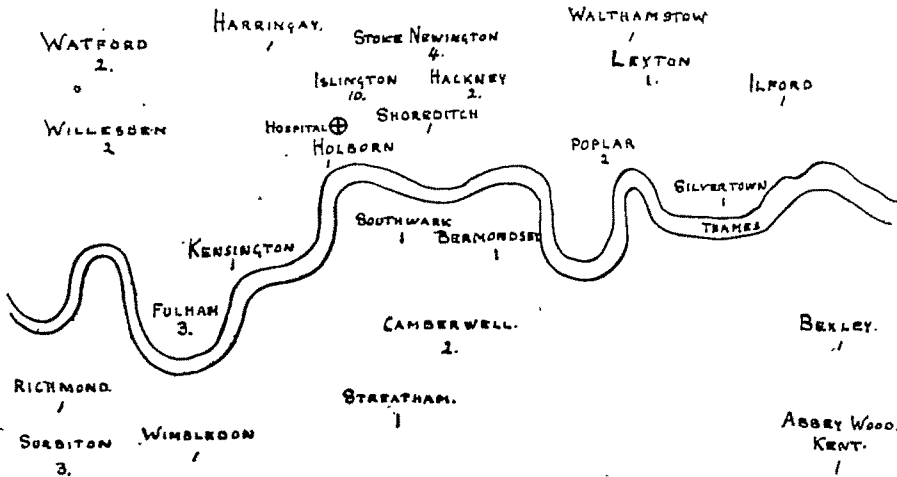


CHART. SHOWING DISTRIBUTION OF 45 CASES OF POLIOMYELITIS COLLECTED AT HOSPITAL MARKED ⊕ THE ONSET OF WHICH OCCURRED DURING THE YEAR 1904.

FIG. 10.

Map of London district, showing the distribution of forty-five cases of poliomyelitis collected at two hospitals. The onset of the disease occurred during 1904.

During the year 1904 I collected at the Children's Hospital some 45 cases of infantile paralysis. I have charted them in the districts in which they occurred. The chart has no special value except to show that the disease is fairly evenly distributed over all London areas (fig. 10). Ten of the cases occurred in the Islington District, but considering the position of the hospitals at which the cases were collected—i.e., National Hospital, Queen Square, and Children's Hospital, Great Ormond Street—it would be from this district that cases would be likely to come. So far as I know all these were isolated cases. With regard to the month of incidence, these few figures bear out what has

been shown in all larger statistics—viz., that by far the larger number of cases occur in the month of August (fig. 11).

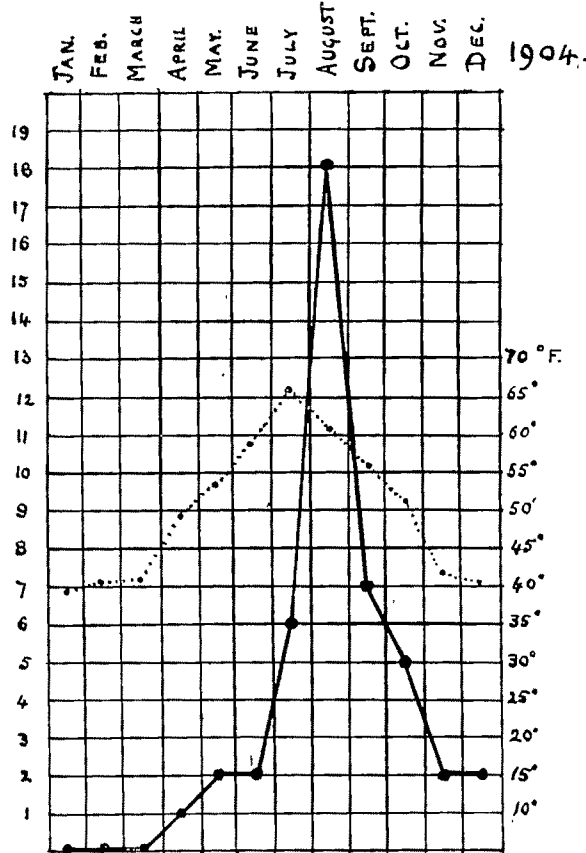


FIG. 11.

Chart showing the month of onset of forty-five cases of poliomyelitis occurring in London during the year 1904. The dotted line shows the mean monthly temperature for the year. These cases were collected at the National Hospital, Queen Square, and the Children's Hospital, Great Ormond Street.

(VII) CONCLUSION.

From the evidence which has been brought forward one is justified in regarding poliomyelitis as an infective disease occurring in epidemic form during the months of July, August and September. It tends to

affect children rather than adults. It is probably communicated from person to person, or may be carried by a person who presents no sign of the disease.

The resemblance of the disease to rabies suggests the possibility of some animal infection, but none has yet been found. The disease can be communicated to the monkey, and passed from monkey to monkey. The infectivity of the disease is not great, for many persons in the closest contact with the infected escape, and monkeys living in the same cage with infected monkeys fail to contract the disease. But little is known of the incidence of the disease in London. That it occurs every summer, and with greater frequency in some years than others, is known. But it is not known if it affects one district more than another.

It will, I think, be admitted that a disease should be notifiable whenever there is liability of its being transmitted from person to person, provided that the disease itself or its sequelæ are a serious detriment to health, or a danger to life. That poliomyelitis is detrimental to health no one will deny.

That poliomyelitis can be, and is, transmitted from patient to patient has been made evident in all the recent epidemics investigated.

The advantages of notification are great. It will lead to the general recognition that the disease is infective, and will tend to prevent its dissemination by contact. Notification will show the prevalence of the disease, and the investigation which should follow must throw light both on the cause and means by which the disease is disseminated.

The infectivity of the disease is not great and the isolation of the infected should diminish the incidence of the disease on the community, and thus prevent the effects which are so disastrous to the usefulness and happiness of many lives.

POSTSCRIPT.—Since the above paper was written the accounts of two other epidemics have been brought to my notice. The first of these occurred in Cuba in 1909 and affected 140 individuals. In seventy-two cases in which the race was specified, sixty were whites, four were mestizos, and eight were negroes.

The second occurred in the Island of Nauru in Melanesia in 1910. The interest attaching to these two epidemics is that they are the first to be recorded within the Tropics.

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MÜLLER. Nauru Epidemic, 1910. *Arch. f. Schiffs. u. Tropen Hyg.*, 1910, xiv.

LIST OF EPIDEMICS OF POLIOMYELITIS.

Year	Author	Town or village	Country	Number of cases	Number of deaths	Mortality percentage
1881	Bergenholtz ...	Umea ...	Sweden ...	18	—	—
1893	Buchelli ...	Arenzano ...	Italy ...	5	2	—
1886	Cordier ...	Foy ...	France ...	13	4	—
1886	Leegard Oxholm ...	Mandal ...	Norway ...	9	2	—
1886	Strümpell ...		Germany ...	3	—	—
1887	Medin ...	Stockholm ...	Sweden ...	44	3	—
1889	Briegleb ...	Turingen ...	Germany ...	5	—	—
1893	Andre ...	S. Girons ...	France ...	4	—	—
1894	Brackett ...	North Adams, Massachusetts	U.S.A. ...	10	—	—
1894	Caverly, Macphail ...	Rutland, Massachusetts	„ ...	192	18	—
1895	Buchelli ...	Ravecca ...	Italy ...	17	—	—
1895	Medin ...	Stockholm ...	Sweden ...	21	—	—
1896	Pierracini ...	Florence ...	Italy ...	7	—	—
1896	Altman ...	Port Lincoln ...	Australia ...	14	—	—
1896	Bondurat ...	Alabama ...	U.S.A. ...	15	—	—
1896	Pasteur ...	Much Hadham ...	England ...	7	—	—
1896	Taylor ...	Cherry Field ...	Maine, U.S.A. ...	7	1	—
1897	Buchelli ...	Genoa ...	Italy ...	17	—	—
1897	Pleuss ...	Kiel ...	Germany ...	4	—	—
1897	Taylor ...	New York ...	U.S.A. ...	12	—	—
1897	Fabis ...	Conegliano ...	Italy ...	9	—	—
1898	„ ...	„ ...	„ ...	13	—	—
1898	Auerbach ...	Frankfurt ...	Germany ...	15	—	—
1898	Zappert ...	Vienna ...	Austria ...	42	—	—
1899	Leegaard ...	Bratsburg ...	Norway ...	64	2	—
1899	Mackenzie ...	New York ...	U.S.A. ...	80	1	—
1899	Newmark ...	San Joaquin ...	California ...	4	—	—
1899	Wickman ...	Stockholm ...	Sweden ...	54	4	—
1900	Painter ...	Gloucester, Massachusetts	U.S.A. ...	32	1	—
1901	Woods ...	San Francisco ...	California ...	55	—	—
1902	Private information	Pietermaritzburg	S. Africa ...	—	—	—
1903	{ Bergendal } { Wickman }	Goteborg ...	Sweden ...	20	—	—
1903	Harbitz and Scheel	„ ...	„ ...	„	„	„
1906	Giersvold ...	„ ...	} Norway ...	1,151	167	—
1903	Lorenzelli ...	Parma ...	Italy ...	26	—	—
1904	Ham ...	Brisbane ...	Australia ...	108	4	—
1904	Naunestadt ...	Fredrickshad ...	Norway ...	41	6	—
1904	Platou ...	Aafjorden ...	„ ...	20	6	—
1905	Giersvold ...	„ ...	„ ...	486	69	—
1905	Wickman ...	„ ...	Sweden ...	1,031	145	12.2
1905	Harbitz and Scheel	„ ...	Norway ...	283	42	—
1906	„ „	„ ...	„ ...	334	34	—
1906	{ Nyman } { Wickman }	Smedjebacken ...	Sweden ...	50	5	—
1907	Lovett ...	Massachusetts	U.S.A. ...	234	—	—
1907	Starr ...	New York ...	„ ...	2,000	—	7
1907	Stephens ...	Victoria ...	Australia ...	135	—	4.5
1908	Davis ...	St. Paul's ...	U.S.A. ...	200	—	—
1908	Hoffmann ...	Heidelberg ...	Germany ...	86	—	—
1908	Löcker ...	Steyr ...	Austria ...	68	—	11.7
1908	Lovett ...	Massachusetts	U.S.A. ...	186	—	—
1908	Koplik ...	New York ...	„ ...	1,200	—	—
1908	Krause ...	Westphalia ...	Germany ...	100	9	9
1908	Treves ...	Upminster ...	England ...	8	—	—

LIST OF EPIDEMICS OF POLIOMYELITIS—(continued).

Year	Author	Town or village	Country	Number of cases	Number of deaths	Mortality percentage
1908	Wiley and Dardem	Salem	Virginia, U.S.A.	25	3	—
1908	Zappert	Vienna	Austria ...	266	14	—
1908	Lindner and Mally	Steyr	" ...	96	16	16
1909	Jogichess	St. Petersburg ...	Russia ...	26	—	—
1909	Lovett	Massachusetts ...	U.S.A. ...	923	—	—
1909	Netter	Paris	France ...	100	5	5
1909	Parker	Bristol	England ...	37	2	6
1909	Peiper	Pommern	Germany ...	51	6	11.7
1909	Fürntratt	Steiermark	Austria ...	493	—	13
1909	Potpeschnigg	"	" ...	493	—	13
1909	Reckzeh	Westphalia	Germany ...	500	—	13
1909	Shidler	Nebraska	U.S.A. ...	200	—	7.5
1909	Spieler	Vienna	Austria ...	44	2	—
1909	Stiefler	Linz and Urfahr ...	" ...	77	—	—
1910	Beard	Carlisle	England ...	34	5	—
1910	Currie and Bramwell	Tillicoultry	Scotland ...	5	—	—
1910	Garrow	Barrow-in-Furness	England ...	37	—	—
1910	"	Maryport	" ...	13	2	—
1910	Hagenbach	Basle	Switzerland ...	19	—	—
1910	Public Health Report	"	U.S.A. ...	5,093	825	13.75
1910	Joint Report ...	Columbia	U.S.A. ...	506	16	—

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[Notes on a book under this heading do not preclude a subsequent review.]

Klinischer Beitrag zur Frage der Alkoholpsychosen. Von Dr. WILHELM STÖCKER. S. 298. Jena: Fischer, 1910.

The author started with the intention of following up the subsequent history of patients admitted to the clinic for mental diseases in Erlangen as cases of "delirium potatorum." He discovered that some other psychosis, which had nothing to do with alcohol, usually underlay the alcoholic delirium; in the majority of cases alcoholic excess was a symptom of some mental defect or definite psychosis. Ninety ex-patients were visited in their own homes. Of these over a third turned out to be epileptics who drank: next in frequency came cases of maniacal-depressive insanity; fourteen were instances of dementia præcox, and nine suffered from some other well-recognized psychosis. Of the remaining five patients one was not a case of alcohol at all but of an acute specific fever, and four were suspicious and difficult to investigate. The histories are well given and the book excellently arranged to display the author's contention that alcoholic excess, associated with insanity, is usually symptomatic of some well-known underlying psychosis.

Die Melancholiefrage. Referat erstattet auf der 40 Versammlung der Südwestdeutschen Irrenärzte in Heilbronn am 6. November, 1909. Von Professor Dr. A. HOCH. S. 14. Leipzig: Barth, 1910.

An excellent statement and criticism of the present views on melancholia and its relation to maniacal-depressive insanity and other psychoses. The author believes that, apart from the organic insanities, typical instances of any form of psychosis are less common the more carefully cases are investigated; individual differences obscure the outlines of the type, and make it impossible to say exactly to what group the patient belongs. But there can never be any doubt that, at any one moment, the patient is in a maniacal, melancholic or katatonic condition. These conditions, like hypochondria, neurasthenia and hysteria, are psychical states, not diseases.

Leitfaden der experimentellen Psychopathologie. Von Dr. ADAELBERT GREGOR. S. 222. Berlin: Karger, 1910.

A series of lectures on the methods of psychophysical examination applicable in cases of mental disease. The author describes the results of investigations on reaction-time, perception, association, memory, attention, and general intelligence. He assumes that the apparatus used in these experiments is familiar to the reader, and thus confines the use of his work to experts; but no one should attempt to apply psychophysical tests in the insane without consulting this book and making himself familiar with the results already obtained.

Contribution à l'Etude de l'Aliénation mentale dans l'Armée suisse et dans les Armées étrangères. Par FRANÇOIS NAVILLE. P. 184. Genève: Kündig, 1910.

Every Swiss citizen is called to arms at 20, and before he is accepted as a recruit a complete examination is made of his bodily and intellectual fitness for service. In this way many epileptics, alcoholics and congenitally feeble-minded are discovered who would otherwise have remained unknown. After passing through the "school for recruits," each man is passed into a corps and serves for eighteen days every two years up to the age of 35. In this way the sanitary service of the army has the opportunity of watching the mental state of the whole male population from youth to middle age. This work gives a short account of the various psychoses which are revealed in this way.

Nervensystem und Insolation. Von Dr. F. A. Steinhausen. S. 163. Berlin: Hirschwald, 1910.

The author, who was for some years with the 16th Army Corps in Metz, has put together in handy form his deductions from over 500 cases of sunstroke. He denies the existence of "heatstroke" without sun; the sun and not the heat of the atmosphere is the active agent in the disease. Hyperpyrexia is a common symptom, but not the cause of the manifestations, which may assume six forms: (1) Cases without changes in consciousness, the least fatal variety; (2) coma; (3) epileptiform or convulsive attacks; (4) delirium, by far the most fatal form; (5) a condition associated with local signs, such as hemiplegia, optic neuritis, &c., which is spoken of as the "encephalitic" form; (6) the dream state (*Dämmerzustand*). Then follow chapters on the etiological factors, such as the effect of alcohol on the neuroses which follow sunstroke, on prophylaxis and therapeutics, and this practical little book closes with an excellent index.

L'Evolution de la Mémoire. Par HENRI PIÉRON. Pp. 355, orné de 20 figures. Paris: Flammarion, 1910.

An excellently arranged account of recent work and views on memory. The first book deals with persistent rhythms, the second with memory in animals, and the third with memory in man. Recent experiments on habits and adaptation in animals are concisely summarized and the references are given with remarkable fulness.

Diagnostik der Nervenkrankheiten. Von Dr. L. E. BREGMAN. Mit einem Geleitwort von Hofrat Prof. Dr. H. OBERSTEINER. S. 535. Mit 193 Abbildungen und 2 Tabellen. Berlin: Karger, 1911.

A compilation of the various signs and symptoms which may accompany lesions of the nervous system, considered seriatim. It is too elaborate for the physician who has no special knowledge of nervous disease, and contains nothing that is not well known to every neurologist.

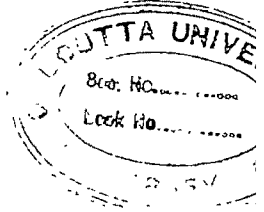
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Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I. to XXIII. inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

[NOVEMBER, 1911.]



BRAIN.

PARTS II and III, VOL. 34.

Original Articles and Clinical Cases.

THE INBORN FACTORS OF NERVOUS AND MENTAL DISEASE.

BY F. W. MOTT, M.D., F.R.S.

Pathologist to the London County Asylums; Physician to Charing Cross Hospital.

INTRODUCTION.

THE inborn factors of nervous and mental diseases having for some time past occupied my attention in my capacity as Pathologist to the London County Asylums, I feel I could not do better than make this the subject of my address to you to-night. Every neurologist recognizes the importance of the inborn factor in the production of neuroses and psychoses, and in certain degenerative conditions of the nervous system, which Gowers has designated under the collective term of abiotrophies. Before, however, I consider the subject of transmission of nervous and mental diseases permit me to direct your attention very briefly to the current theories of heredity.

Heredity is essentially a mechanism for preserving that which has been won by progressive evolution and natural selection, and every species has probably reached an unchangeable type in which the inheritance has become more or less perfected and fixed; there is in consequence continuity of the germ-plasm. If we argue that arrival of the fittest preceded survival of the fittest, then it may be asked what occasioned this arrival—to term it a sport or fortuitous variation is begging the question, for an effect always owns a cause, although we may not be able to discover it.

By the laws of heredity the germ-plasm has acquired a fixity in stability of characters of the species; the race, the sex, and to a much less degree of ancestral stocks, thus preventing the organs and structures

of the body from varying in any considerable degree from the normal average, which has been attained by evolution. In fact the only organ now in which the transmission of a functional hypertrophy could be useful is perhaps the human brain, and it is extremely doubtful according to Kohlbrugge and other anthropologists whether this ever takes place.

Functional hypertrophies of body-tissues are useful in establishing an equilibrium according to physiological requirements of the environment; they are limited in their development, and are not transmitted in the Lamarckian sense; if they were, the stability of the germ-plasm in respect to the biochemical and dynamic equilibrium existing between all the organs and tissues of the body would be upset, and the product of evolution of countless ages endangered.

A functional hypertrophy in successive generations does not imply transmission of an acquired character, as observation and experiment show that it is the result of the persistence of the environmental conditions which led to the physiological adaptation.

THE THEORIES OF HEREDITY.

The "Law of Ancestral Inheritance" of Galton marks as great a step of progress in our knowledge of heredity as that which we owe to another great investigator, Gregor Mendel, who was born in the same year, 1822. Galton's law supposes that every ancestor of a particular individual contributes its quota to the heritable qualities of the individual. The law also states that the average amount of resemblance between an individual and any particular ancestor is capable of definite numerical expression. Thus the mean amount of correlation between (1) the two parents and the offspring, (2) the four grandparents and the offspring, and (3) the great grandparents and the offspring, and so on backwards in the ancestral lineage, diminishes in a geometrical series one-half, one-quarter, one-eighth, which is the same for all organisms and their characters.

Pearson represents a more rapidly diminishing series: (1) For the two parents, 0.6244; for the grandparents, 0.1988; for the great grandparents, 0.0630, &c. There is thus a mosaic of ancestral qualities. It is probable that the above represents correctly the average total contributions of ancestors when applied to the race as a whole, but it cannot be applied to individuals; for according to Mendel's theory of inheritance certain ancestors may contribute nothing to the constitution of certain offspring in respect to certain characters. Galton

himself admits this in his work on *Natural Inheritance*: thus he says:—

“Though one half of every child may be said to be derived from either parent, yet he may receive a heritage from a distant progenitor that neither of his parents possessed as personal characteristics.” Again: “All living beings are individuals in one respect, composite in another. We seem to inherit bit by bit this element from one progenitor, that from another; in the process of transmission by inheritance elements derived from the same ancestor are apt to appear in large

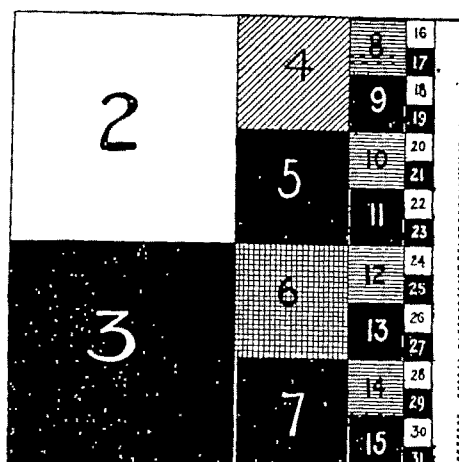


FIG. 1.¹—Diagram illustrating Galton's "Law of Ancestral Inheritance." (After Galton.) The figure was originally due to Mr. A. J. Meston. (*The Horseman*, Chicago, December 28, 1897.)

groups, just as if they had clung together in the pre-embryonic stage, as perhaps they did. They form what is well expressed by the word 'traits,' traits of feature and character, that is to say, continuous features and not isolated points."

I will ask you to remember these conclusions of Galton, for they have a most important bearing upon the subject I shall discuss more fully later. Likewise let me call your attention to Galton's remarkable work on twins; he showed by a collective investigation the great importance of the inborn factors in respect to character; for he found that twins with similar inborn characters remained similar when in later life they lived under different environmental conditions; likewise

¹ This figure and fig. 8 have been taken from Arthur Thomson's "Heredity," with the kind permission of the author and John Murray, the publisher.

twins with dissimilar inborn characters remained dissimilar when brought up under similar environmental conditions.

Galton also made a statistical inquiry on good and bad tempers in English families, and as a result of this inquiry he says: "It now becomes clear enough and may be taken for granted that the tempers of progenitors do not readily blend in the offspring, but that some of the children take mainly after one of them, some after another, but with a few threads, as it were, of various ancestral tempers woven in, which occasionally manifest themselves. If no other influences intervened the tempers in the children of the same family would on this account be almost as varied as those of their ancestors." To recapitulate briefly, one set of influences tends to mix good and bad tempers in a family at haphazard; another tends to assimilate them, so that they shall all be good or all be bad; a third set tends to divide each family into contracted portions.

These facts ascertained by Galton are of great interest in connexion with the inheritance of the predisposition to neuroses and psychoses. Galton's law of regression again serves to explain many facts regarding the inheritance of feeble-mindedness as well as ability. In respect to the latter, Galton showed that only a few out of many children would be likely to differ from mediocrity, as their mid-parent, and still fewer would differ as widely as the more exceptional of the two parents. The more bountifully the parent is gifted by Nature the more rare will be his good fortune if he begets a son as richly endowed as himself, and still more so if he begets a son who is endowed yet more largely. But the law is even-handed, it levies an equal succession-tax on the succession of badness as of goodness. If it discourages the extravagant hopes of a gifted parent, that his children will inherit all his powers, it no less discountenances extravagant fears that they will inherit all his weaknesses and tendencies to disease.

This tendency to revert to the normal average of the race is thus a great factor in heredity. Amphimixis, or the blending of the inheritance of two individuals, is claimed by Weismann as the great factor in the production of variation and evolution, but when there is a dynamic equilibrium of the germ-plasm established for a species amphimixis would act in the opposite way in arresting the perpetuation of a variation.

MENDELISM.

The Mendelian doctrine of the gametic segregation of alternate unit-characters has recently been the subject of considerable discussion in

relation to its application to the transmission of inherited disease; it is necessary therefore for me briefly to refer to Mendel's work on hybridization.

Mendel crossed tall peas with short peas, smooth with wrinkled seeds, yellow-coated with green-coated seeds. It will suffice if I refer to the first experiment of crossing tall with dwarf peas, cited by Bateson in the discussion on heredity held by the Royal Society of Medicine a few years ago. To prevent self-fertilization Mendel cut off the stamens of one variety, then artificially fertilized with the pollen collected from the other. When the seeds of this plant which had been artificially fertilized with the other were sown, he had a proportion of three tall plants to one short. These plants were allowed to self-fertilize and the seeds when sown gave the following results: the dwarf produced only dwarf, and one of the three tall plants produced only tall plants, whereas two of the tall plants, self-fertilized, produced proportionally three tall plants to one dwarf. Now Mendel explained it in this way. In F^1 , where a tall-bearing gamete is crossed with a short-bearing gamete, the chances are

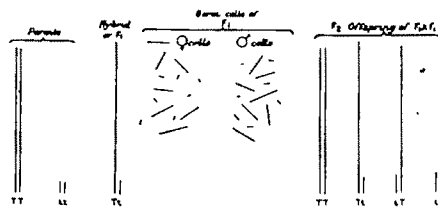


FIG. 2.—A diagrammatic representation of the germ-cells of the tall and short plants, and of their combinations.

that tall will meet with short twice as often as short will meet with short or tall with tall, and this is what does happen, for in F^2 after self-fertilization there are three tall plants to one short, but two of these tall plants are hybrids and have characters of tallness and shortness in each gamete. This is shown by the fact that if these hybrids of F^2 generation are self-fertilized again we shall have in F^3 the same result as in F^1 —viz., three tall and one short (fig. 2).

Tallness is the dominant character, shortness is the recessive, but the results of the experiments show that there is no blending of these alternate unit characters. The character which is prepotent in the hybrid offspring is termed dominant, the alternate latent character is recessive; for this case tallness is dominant, shortness recessive. If one of the extracted normals, whether tall or short, be taken and the

seeds sown, only tall or short plants can be obtained, and no amount of selection of the seeds of the shortest of the tall plants or the tallest of the short will convert a short into a tall or a tall into a short.

Instead of taking tall and short characters in the crossing we might take pigment and absence of pigment; we could then illustrate Mendelism with draughts, as this photograph shows. Professor Bateson said at this discussion: "I shall have no difficulty in showing you that the conclusions to which Mendel came are applicable in many cases to the descent of disease or congenital deformity." Pearson admitted the great importance of Mendel's work, but considered it was limited to

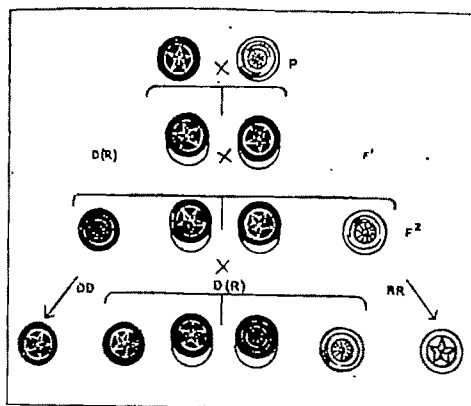


FIG. 8.—Diagram, photographed from draughts, to illustrate Mendel's Law. (After Bateson.) First line (P), a black dominant and a white recessive. Second line (F¹), the hybrid offspring, D(R), the black patent, the white latent below. Third line (F²), one "pure" black, two "impure" blacks, and one "pure" white, 1DD+2D(R)+1RR. Fourth line, pure extracted dominant to the extreme left, pure extracted recessive to the extreme right; in the middle, as usual, 1DD+2D(R)+1RR.

the observation of gametic segregation; he was sure that it was too early in the day to assert that all the Mendelian doctrine holds for man, and he would even go a step further in questioning whether it holds for plants and animals.

Nettleship, on the other hand, takes up a much broader view of the application of Mendelism to human inheritance. He points out that the Mendelian theory refers to well-defined characters taken singly and separately. Such are in peas, for example, tallness or shortness of stems, greenness or yellowness of seeds, smoothness or wrinkling of seed-coats. But complexities are introduced when two characters are permanently associated or inseparably linked or coupled in descent and in other ways. Even in such cases, however, careful analysis appears

often to *succeed* in bringing the numerical results of breeding experiments that appeared hopelessly confused into line with Mendelian requirements. It is likely enough that some such associations and interactions between pathological factors may explain certain of the irregular proportions of diseased to normal in pedigrees of human disease.

The Transmission of Disease.

Nervous and other diseases are not all transmitted in the same way; there are some which are transmitted in successive generations by both

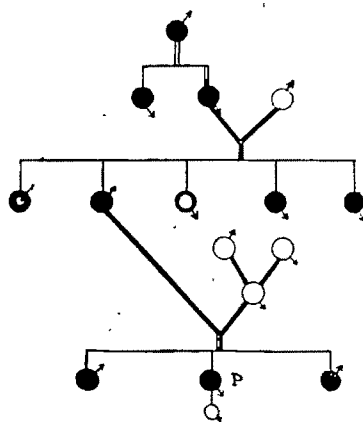


FIG. 4.—Paternal great grandfather suffered with chorea—also paternal grandmother and sister. Two paternal aunts and father suffered with chorea and died in asylums or infirmary—brother physically unsound and sister suffered with nervous disease. P., the patient, chorea and insane, one brother in asylum and one died. It will be observed that the maternal side is quite free from any taint. Black circles indicate members of the stock affected with chorea; shaded circle, dead in infancy; circle with deep black rim, physically unsound; black circle with white centre, physically unsound.

sexes, sometimes equally, sometimes unequally. The majority of human heritable diseases, or tendencies to disease, are transmitted in this manner. Many pedigrees have been recorded which show that some well-defined abnormal condition or defect may descend uninterruptedly through five or six generations, and even a few pedigrees illustrating this mode of transmission for seven or eight generations have been recorded. Among the diseases belonging to this group may be mentioned Huntington's chorea, of which I will show you a pedigree of four generations; and through the courtesy of Dr. Bond, of Long Grove Asylum, I have had the opportunity of obtaining the central nervous system of the youngest member of this diseased stock (fig. 4). Other

hereditary conditions which may be mentioned as belonging to this group are occasionally instances of hereditary ataxy, such as the pedigree of a stock recorded by Sanger Brown; other examples are to be found in angioneurotic oedema, and certain eye conditions such as retinitis pigmentosa, senile cataract, coralliform cataract, nuclear or reticular keratitis, and, lastly, congenital stationary night-blindness—a most remarkable pedigree of which has been constructed by Cunier and Nettleship. I am showing this pedigree because it illustrates the fact that a variation or mutation is not easily swamped out by dilution with the normal. This remarkable pedigree comprises nearly 2,000 individuals and extends back for ten generations; it commenced, so far as is known, with Jean Nougaret, born 1637; and subsequently 135 descendants of this individual were affected with congenital stationary night-blindness. Mendelians claim this as a proof of Mendelism, and assert that the congenital defect is dominant and the normal is recessive in this pedigree. Whenever normal parents of this stock have married—and in this family intermarriages between extracted normals have occurred—the offspring is always normal; at any rate this pedigree proves gametic segregation of alternate unit-characters, whether numerically it follows Mendel's doctrines or not.

Another mode of transmission is termed sex-limitation; in this the transmission is not only discontinuous or interrupted in successive generations, but the disease is limited to one sex; and in addition there is this extraordinary peculiarity, the disease is transmitted by the sex in which the disease does not appear. It is the males who are affected in these hereditary sex-limited diseases; it is the females who transmit it.

The most striking examples of this mode of inheritance are Daltonism, or colour-blindness, and hæmophilia. I show a lantern-slide of Daltonism exhibiting this mode of transmission. As examples of nervous affections which are transmitted in this way, I may mention pseudohypertrophic paralysis and certain allied conditions, as well as Leber's disease, optic atrophy. Some authorities dispute the sex-limitation of these diseases; in any case it may be asserted with confidence that these diseases are almost, if not entirely, sex-limited.

If defects, abnormalities, diseases, or predispositions to disease are continually arising by germinal variations, and are not readily swamped out by dilution with normal stocks in a series of generations, what prevents every stock of the whole race becoming affected and degenerated? Before attempting to answer this question, I will call

your attention to the neuroses and psychoses and their inheritance, or, rather, tendency to inheritance, owing to the inborn factor of what we may term the neuropathic tendency existing in one or both of the parental stocks.

It has been shown by Galton, Pearson, and others that just as physical characters are inherited from ancestral stocks, so likewise are the mental characters; and Galton, in his work on Natural Inheritance, has shown that the tempers of ancestors may be repeated in the descendants; there is therefore gametic segregation of temperaments, as there is gametic segregation of physical characters; so that in a family a child may resemble the father or the mother, or, perhaps, some more distant relative, in its physical characters, or in its temperament or mental qualities. Such being the case, we can understand why, in a family, the parental stocks of which exhibit neuropathic tendencies, only certain individual offspring may inherit those tendencies.

Nature and Nurture.

No child is born insane, although it may be born feeble-minded, from actual cerebral deficiency. In every case of neurosis or psychosis, we should endeavour to ascertain what the individual was born with (nature), and what has happened at or after birth (nurture). To ascertain the inborn factor, it is necessary to study the parental characters and those of the parental stocks. To collect statistics merely relating to the question of certifiable insanity or epileptic fits is quite insufficient, for the neuropathic tendency manifests itself in multiform ways, and it is necessary to seek the first stages and less obvious conditions of degeneration in a stock. Morel, who studied this question fifty years ago, pointed out that nervous irritable weakness, that which we term the neurotic temperament, may be the first evidence of a progressive degeneration in the stock.

The morbid neurotic temperament may be manifested in a variety of ways by the conduct and behaviour observed in various members of the stock. The signs of degeneracy which may be exhibited are self-centred narrow-mindedness in religious beliefs, fanaticism, mysticism, and an unwholesome contempt for traditional customs, social usages, and morality, often combined with a selfish, self-seeking, vain spirit of spurious culture, or by a false sentimental altruism, or by eccentricities of all kinds; such signs of degeneracy are often combined with talent, and often genius, but the brilliant intellectual qualities of a degenerate are invariably associated with either a lack of moral sense or of sound judgment and highest control (fig. 5).

An unsound stock may have successful men in the eyes of the world, but these may really form the first step in the process of degeneration; for the avarice and moral guile which made them "pillars of society" may come out in the next generation as gross criminality or insanity.

The melancholic temperament.—I have often found in the collecting of pedigrees that degeneracy and insanity in a stock are preceded by, or associated with, the existence of individuals possessing the melancholic, suspicious, hypochondriacal, despondent, gloomy, self-regarding

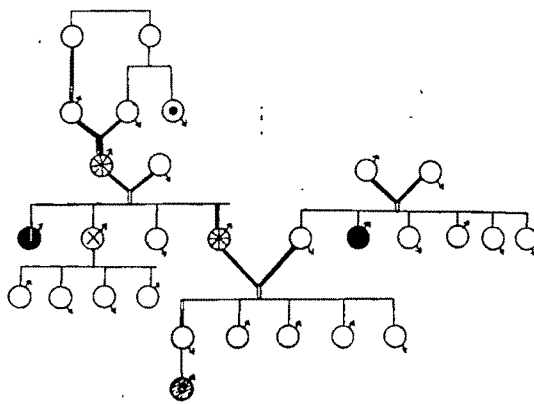


FIG. 5.—A pedigree illustrating marriage of first cousins; a genius the product, who married a healthy woman, and the family consisted of an eldest son insane, black figure; a second son committed suicide, X; a daughter healthy, and fourth son genius, figure with star. This man was a genius, but had an extremely well-balanced mind; all his five children are healthy.

temperament: and it is not uncommon for suicide of one or more members of the stock in successive generations to occur. The melancholic temperament may, however, be associated with unusual abilities and great power of attention and concentration. With these temperamental evidences of degeneracy of a stock may be hysteria, hypochondriasis, psychasthenia, neurasthenia, migraine, petit mal, or neuroses of an epileptic character, unrecognized, because not manifesting the characteristic fits of the major form of the disease—e.g., epilepsy may present the form of automatism and sudden criminal impulsiveness. Consequently, in taking a family history, there are many possibilities of missing the inborn factor of a neurosis or psychosis, even though a considerable amount of care and industry be expended, combined with intelligent co-operation on the part of the friends (figs. 6 and 7).

I have purposely refrained from mentioning alcoholic intemperance

and the habit of drug-taking so common in degenerates of all kinds; the habit may be the cause or the result of the degeneracy. I am, however, of opinion that various causes, such as alcoholism, infective

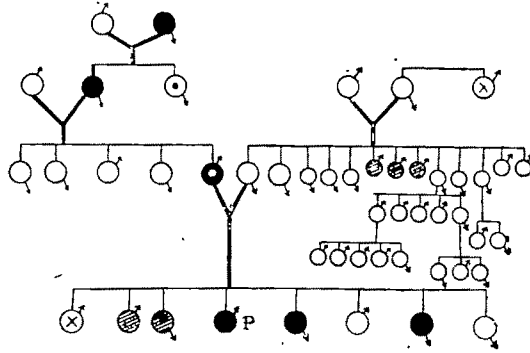


FIG. 6.—Four generations; all the unsound taint from one stock, in the fourth generation. P., patient, murderer and lunatic; the eldest brother committed suicide and there were two sisters insane; two children died young (shaded circles), and a boy and girl healthy. The ages of onset not known, except that the murderer was only a lad.

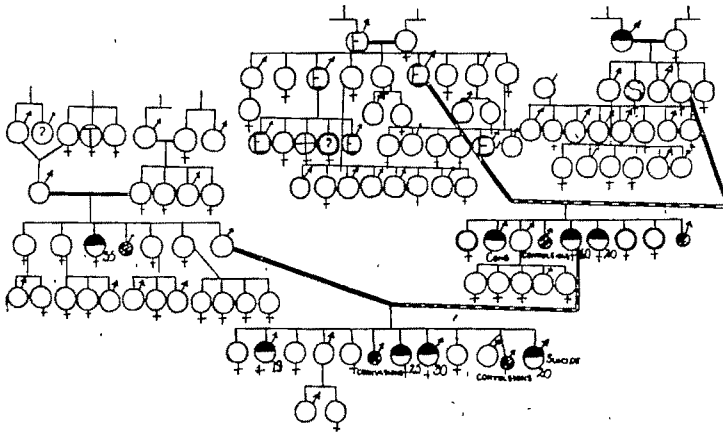


FIG. 7.—Pedigree by Dr. Wilson White. E, epileptic; S, suicide; cross in circle, drink; half black, insane; those with a star, found dead. Anticipation is shown, but the interesting part of this pedigree is that, in the fourth generation, four out of twelve born alive are insane at an early age, probably dementia præcox; two died in infancy of convulsions. The deep-black-rimmed circles are neuroses or nervous disease. It will be observed that the unsound taint came especially from the maternal side. Careful inquiry showed that most of the sane members of this stock were of a melancholic temperament. On the father's side there was very little hereditary taint; only one male insane. This stock, generally speaking, had members with a sanguine temperament. The sound members of the fourth generation probably inherited more from this stock than the mother's; the converse with the unsound members.

diseases, auto-intoxications, physical injury, especially head injuries and shocks, emotional shock, sexual excesses, and unnatural practices are too often wrongly assigned as the *sole* cause of nervous and mental disease,

to the neglect of the inborn factor (fig. 8). In nervous and mental, as in bodily disease, there are nearly always two factors—viz., the soil and the seed, the inborn and the acquired environmental. There are individuals born of sound stocks, that no acquired conditions—e.g., drink, poisons engendered within the body or taken from without, head injuries, emotional shock, distress and even profound misery and destitution combined—can render insane. There are others, and these are generally from a neuropathic stock, whose mental equilibrium may be disturbed by any one of these conditions or very frequently, as my further observations will show, without any apparent cause except the conditions appertaining to the sexual functions in adolescence, the puerperium, and the involutional or climacteric period.

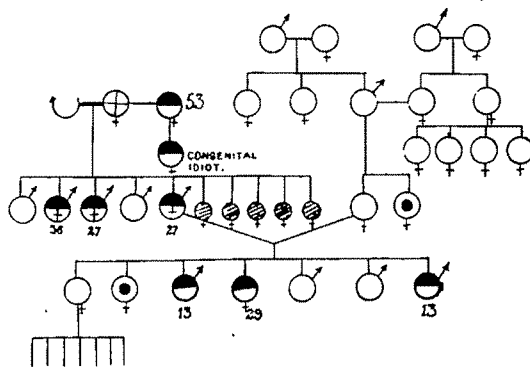


FIG. 8.—A family of drunken and insane people. The figures with half-black circles are insane; the same with the cross indicates drink and insanity. The clear circle with a cross, drink only in the history. The heredity begins with a drunken woman; in the next generation there are two normal, three drunk and insane beginning at an earlier age, and the five youngest die in infancy or are born dead. One of the drunk and insane marries a healthy woman of a good sound stock: there are six children; three are insane in early life, three are healthy; the eldest with seven healthy children; the second clear circle with black centre indicates bodily disease. I used to give this as an instance of drink producing insanity, but after the establishment of the card system I found the sister of the drunken grandmother died in Colney Hatch Asylum after having been there twenty years; her daughter was a congenital imbecile at Leavesden.

I am of opinion that the more time and trouble taken to obtain a history, the more frequently an inborn factor will be found to account partly, if not wholly, for the appearance of insanity in a stock. To take an example, two brothers are at present in Claybury, named Martin and Luther; the notes did not indicate any inborn factor. I interviewed the father, a very intelligent, excitable old man; he told me that he had named his sons Martin and Luther after the defender of the faith. He was a total abstainer, a very religious man; he was formerly a ship's engineer; he left the service because he refused to work on

Sunday, and he laid the ship up rather than do this. He had invented many patents, some of them very clever, and his sons had been engaged with him in these enterprises. He attributed their mental breakdown to business worries on account of the failure of the patents.

Another case I saw in which there were three sisters who were affected with adolescent insanity, in which there was said to be no neuropathic history. I found the father had suffered with petit mal and migrainous attacks, for which he had been attended at the National Hospital.

I could give numbers of instances like this where careful search in apparently non-hereditary cases shows that an inborn factor has existed.

Figs. 5, 6, 7 and 8 illustrate some of these points.

Perhaps one of the worst forms of degeneracy is vagrancy, or inability or absence of desire to exist by individual endeavour. I have

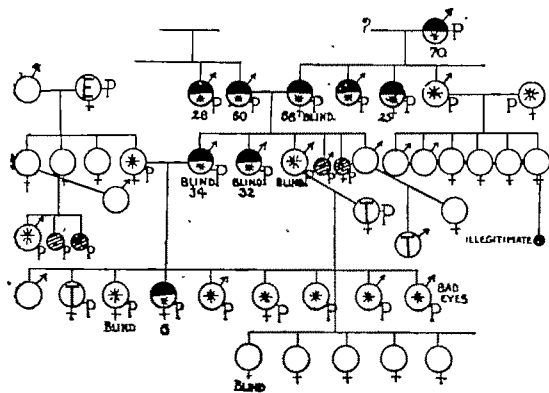


FIG. 9.—Four generations in which P, pauperism, E, epilepsy, tuberculosis, insanity, and drink are shown together with blindness. Mr. Lidbetter, the relieving officer, furnished me with the details of this pedigree.

a number of pedigrees obtained from the relieving officers showing pauperism, drunkenness, insanity and tuberculosis. Here is one of four generations, in which we find a large number of members of the stock who have been in the workhouse infirmary as paupers, or in the asylums; many of them are blind in successive generations: whether this is an hereditary optic atrophy I do not know. (Fig. 9.)

Regression to the Normal.

If defects, abnormalities, diseases, or predispositions to disease are continually arising by germinal variation, and if morphological defects,

as we have seen in the case of congenital stationary night-blindness and other conditions, such as brachydactylism, polydactylism, &c., are not easily swamped out by dilution with normal stocks in a series of generations, what prevents the race becoming more infected by such abnormalities?

There is always the tendency to regression to the normal average of the species and of the race. The germ-plasm of normal stocks is endowed with that dynamic, stable equilibrium which has been fixed for countless ages by evolution in the struggle for existence and survival of the fittest by adaptation to environment. By this means heredity acts as the great fly-wheel in the mechanism of the evolution of the species. Nature has, however, evolved other methods of preventing imperfections and poor mental and physical types from becoming perpetuated. Nature, unmindful of the individual, and mindful only of the species, has adopted a quicker method of weeding out and killing off the poor types; it is by increasing their susceptibility in successive generations to ubiquitous germs or poisons—e.g., tubercle¹ and alcohol. Another of Nature's methods is to intensify the disease or predisposition to disease and to bring it on at an earlier age and even at birth, thus anticipation or antedating renders the unsound members of the stock less able to survive in the struggle for existence by reason of the disease impairing seriously their mental or physical powers. I mean especially the struggle for existence in the sense of Malthus and of Darwin, the struggle for the necessities of life among members of the same species, namely, the human struggle.

The Law of Anticipation.

I am indebted to Mr. Nettleship, who has done so much to advance our knowledge of the hereditary transmission of disease, for calling my attention to this law. He has defined anticipation in hereditary disease as a manifestation of the morbid change at an earlier age either in

¹ "A comparison of the phthisis death-rate at the several age-periods per sane living in London, and per 1,000 of the total living insane population (18,872), resident in the London County Asylums, shows that the mortality from phthisis among the insane is highest at a much earlier age-period than among the sane. At the age-period 45-55, when it reaches its maximum among the sane, it is a question whether the incidence among the insane is much greater than among the sane pauper population. The comparison also shows that the death-rate from phthisis for the insane between the ages of 15-35 is about fifteen times that for the sane for the same age-period. Allowance, however, must be made for the fact that the majority of the inmates of the asylums belong to the poorest classes." This conclusion I arrived at from a careful investigation of "Tuberculosis in the London County Asylums" after five years of notification. The full paper is published in *Archives of Neurology and Psychiatry*, vol. iv, 1909.

members of each succeeding generation as a whole, or in successively born children of one parentage.

Darwin in his "Animals and Plants under Domestication" refers to anticipation thus: "There is a strong tendency to inheritance to disease at corresponding periods of life. When the rule fails, the

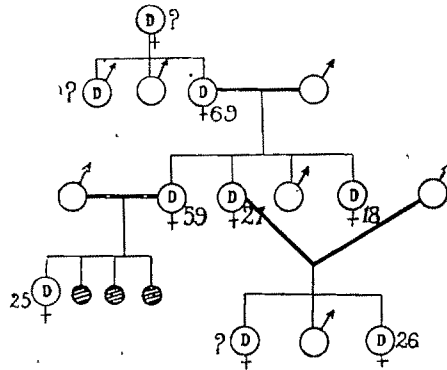


FIG. 10.—Pedigree of diabetes. (After Nettleship.)

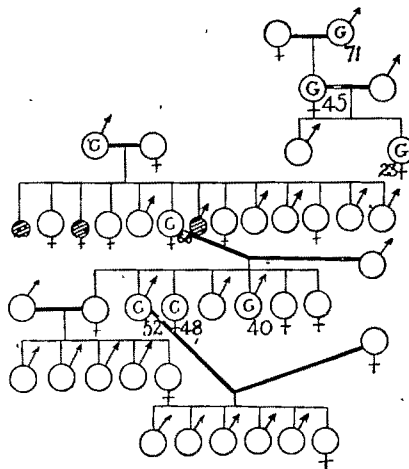


FIG. 11.—Two pedigrees of glaucoma. (After Nettleship.)

disease is apt to come on earlier in the child than in the parent, exceptions in the other direction being much rarer."

Lucas alludes to several cases of inherited disease coming on at an earlier period. Bowman remarks that this frequently occurs with cataract.

Nettleship gives some interesting facts and pedigrees of anticipation in diabetes and glaucoma and he has collected a number of pedigrees in which the age at death is stated in the diabetic children of diabetic parents. Thirteen diabetic children of diabetic parents died at the average age of 25; ten diabetic parents of the above offspring died of diabetes at the average age of 51. Bence Jones, Pavy, and Naunyn recite cases illustrating antedating in hereditary transmission of this disease. Dr. Albert Gray has furnished me with three pedigrees of otosclerosis showing antedating. Nettleship, in his Bowman Lecture, remarks that anticipation appears to occur in phthisis, and he refers to Pollock's "Medical Handbook of Life Assurance," 4th edition, 1895, and Karl Pearson, "A First Study of the Statistics of Pulmonary Tuberculosis," 1907.

From the study of pedigrees, I had, early in my investigations on heredity, often observed that there was a general tendency for insanity not to proceed beyond three generations. There is frequently either a regression to the normal type or the stock dies out. Not infrequently the stock dies out by the inborn tendency to insanity manifesting itself in the form of congenital imbecility, or in the insanity of adolescence. Such patients, especially paupers, are prone to die of tuberculosis; thus rotten twigs are continually dropping off the tree of life. Morel, in 1859, pointed out that progressive uninterrupted transmission leads finally to special degenerative forms, to imbecility and idiocy, and with the diminished capability of propagation of the latter kind the stock therefore gradually becomes extinct.

Antedating and intensification of heritable disease, or predisposition to disease, would not only lead to diminished vital resistance to poisons or germs of disease such as alcohol and tuberculosis, but also, owing to lack of physical and mental ability to obtain the necessities of life, vital resistance is still further diminished, so that the tendency is for the unsound members of the third or fourth generation of a mentally degenerate stock to die at a comparatively early age, of some intercurrent disease, especially tuberculosis, and thus propagation is prevented. Again, the earlier the disease or defect appears, and the more intense its form, the less likely is marriage to occur and offspring to be born; moreover, obvious inherited disease or congenital defect, such as harelip, cleft palate, and even predisposition by inheritance to insanity or epilepsy, interferes with marriage and parentage among the better classes; unfortunately it does not interfere with marriage or mating and parentage among the lowest, most fertile, least desirable classes of the population.

Sterility often accompanies marked mental deficiency, but there is no limit to the fertility of the higher-grade imbecile; in fact, the poorer the stock in mental and physical power and civic worth, the more prolific it is. In our cities and large towns venereal disease sterilizes very soon the great bulk of women who lead immoral lives; this is not so in the country districts, where a weak-minded woman may have a large number of illegitimate children. A great source in my opinion of national degeneracy is the prolific higher-grade imbecile.

Before considering the evidence which I have obtained of this law of anticipation in relation to neuropathic and psychopathic degeneration of stocks, I would like to call your attention to some interesting observations on this subject by Nettleship. He says: "Anticipation or antedating of onset or of completion in a family might be taken to show the transmission of an acquired character. But it probably may be explained as well or better by assuming that certain defects, taints or vices of the system, say of the blood, are not only hereditary in the true or germinal sense, but able to produce toxic agents in the embryo, which have an evil influence on all its cells, and thus so lower their power of resistance that the innate hereditary factor has freer play, and is likely to manifest itself earlier. There may also be toxic agents in the embryo that have no relation to the hereditary vice, but yet may and probably do act in a similar manner as excitants of the disease."

I cannot here discuss the chromosome theory, but it is generally assumed that there is a particulate inheritance derived from the nuclear substance of the male and female germ-cell in the fertilized ovum, and that the nuclear substance derived from each parent is equal in amount. This seems to be proved by the facts observed concerning the reduction of the chromosomes in the process of maturation of the male and female germ-cells. Weismann adopted the chromosome theory of germinal determinants, and Nettleship has modified a diagram of a scheme of transmission by Ziegler. Let us see what it shows.

A represents the male parent; his immature germ-cells have derived their chromosomes, germinal determinants or representative particles (Galton) from his father and mother, and they are respectively represented by different figures. The eight germ-mature chromosomes are reduced to four during maturation, two from each parent; the figures *a-f* indicate the combination of two maternal with two paternal, all diseased, but in different degrees and modes. B represents the female parent, in which there is an inherited taint, but only to a slight degree, coming from the maternal side; in the mature germ-cells only

one containing number 13 will be tainted. C shows some of the results which may arise from the conjugation of $A \times B$.

Assuming the intensity of inheritance is constant for each chromosome or other unit of germ-plasm, but to vary with the number of the germinal units tainted, we have as a result of the mating of these two tainted stocks all degrees of manifestation of ancestral characters from perfect normality to the most profound disease. The more numerous the tainted germinal units the greater will be the chance of the disease appearing in the offspring. On the other hand, the oftener reduction, with its possible random arrangement, has occurred—i.e., the greater the number of generations—the less will be the chance of any particular character finding a place in the inheritance (Nettleship).

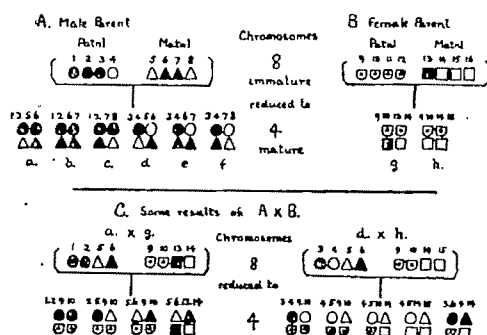


FIG. 12.—Transmission of a defect in different degrees by the same parents.

Certainly this idea of the scheme explains certain facts which have been observed in the pedigrees I have shown; it shows why the offspring of parents derived from two tainted ancestral stocks are more likely to suffer with an intense form of the disease; it shows also why more of the offspring are liable to be affected and it shows why a certain proportion of the offspring may escape entirely; but according to the hypothesis thus advanced it does not explain why only relatively few of the offspring are tainted as compared with the numbers born, even though there be convergent neuropathic inheritance, that is, the germinal determinants of both parents may be largely tainted and yet fewer offspring are affected by the disease than would be expected. In neuroses and psychoses it is not a disease that is transmitted but a predisposition or tendency, and some other factor than the inborn is required to produce the disease. If we ask ourselves the question, How could Nature

Since that time, however, a large number of cases have been added and the total now reaches about 2,800, and on these cases the following statistical investigations have been made.

The material supplied 508 pairs of parent and offspring (from the records of 464 insane parents whose 500 insane offspring have been also resident in the London County Asylums), and in these the age at the time of first attack has been investigated.

The following table is compiled from 217 pairs of father and offspring, and 291 pairs of mother and offspring. The figures denote the percentage of cases whose first attack occurred within the given age-periods.

Age-periods	Father	Offspring	Mother	Offspring
Under 20 years	1.4	26.2	0.6	27.8
20-24	0.4	18.0	3.4	15.7
25-29	1.4	18.0	4.4	18.2
30-34	9.6	13.0	7.8	13.4
35-39	11.5	7.8	9.2	10.0
40-44	9.2	6.4	10.3	5.8
45-49	14.8	6.0	12.0	3.7
50-54	17.5	0.9	12.3	2.4
55-59	13.8	3.7	14.0	1.7
60-64	10.1	—	11.6	1.3
65-69	5.0	—	8.8	—
70-74	4.6	0.4	8.1	—
75-79	0.4	—	1.9	—
80	0.4	—	0.6	—

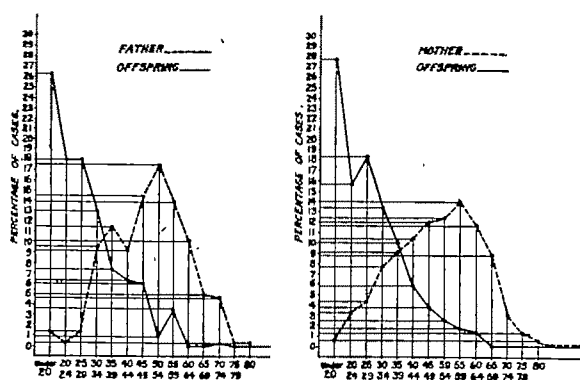


FIG. 13.

These figures are shown graphically in the above diagram, the abscissæ representing the age-periods, and the ordinates the percentage

of cases whose age at the time of first attack falls within the given periods (fig. 13).

Investigating the ages at the time of first attack in the insane offspring of insane parents, I find in the following pairs that 239, or 47·8 per cent., out of 500 offspring had their first attack at or before the age of 25 years :—

Mother—son	51 out of 118 offspring
Mother—daughter	81 „ 170 „
Father—son	45 „ 90 „
Father—daughter	62 „ 122 „
Total	239 out of 500 offspring = 47·8 per cent.

The following table shows the average age at the time of first attack in parent and offspring :—

					AVERAGE AGE	
					Parent	Offspring
120 pairs mother—daughter					49·7	29·3
67 „ mother—son					50·2	30·7
76 „ father—daughter					50·1	30·4
51 „ father—son					51·9	33·1
79 parents, 193 offspring in families with more than 2 insane					47·7	28·7
Total: 393 parents, 427 offspring					49·7	30·0

In addition there were seventy-one parents whose average age was 49 years at the time of first attack, who were associated with imbecile offspring.

Lastly, I find that in 299, or 58·8 per cent., of the 508 pairs of insane parent and offspring, the first attack in the offspring occurred at an age twenty or more years earlier than in the parent; of these 299 instances seventy-three of the offspring were imbeciles.

Collateral Heredity.

The following table is compiled from 193 pairs of uncles and aunts with nieces and nephews in which only collateral heredity is manifested, and 231 pairs of uncles and aunts with nieces or nephews, in which are included those instances where one or both parents of the nieces and nephews are also insane. The figures denote the percentage of cases whose first attack occurred within the given age-periods.

Age-periods	COLLATERAL ONLY		COLLATERAL AND DIRECT	
	Uncle or aunt	Niece or nephew	Uncle or aunt	Niece or nephew
Under 20 years ..	5.2	20.7	5.2	25.5
20-24 ..	8.1	19.2	8.4	17.7
25-29 ..	6.2	18.6	7.8	19.0
30-34 ..	12.9	17.1	14.8	16.1
35-39 ..	11.9	12.4	12.1	11.2
40-44 ..	11.8	5.7	10.4	4.8
45-49 ..	12.4	2.1	12.1	2.6
50-54 ..	14.5	2.1	12.1	1.7
55-59 ..	7.7	1.5	8.6	2.1
60-64 ..	8.8	—	8.2	—
65-69 ..	1.5	0.5	1.7	0.4
70-74 ..	1.0	—	1.3	—
75-79 ..	3.1	—	2.6	—
80 ..	—	—	—	—

These figures are shown graphically in the following diagram, the abscissæ representing the age-periods and the ordinates the percentage of cases whose age at the time of first attack falls within the given periods (fig. 14).

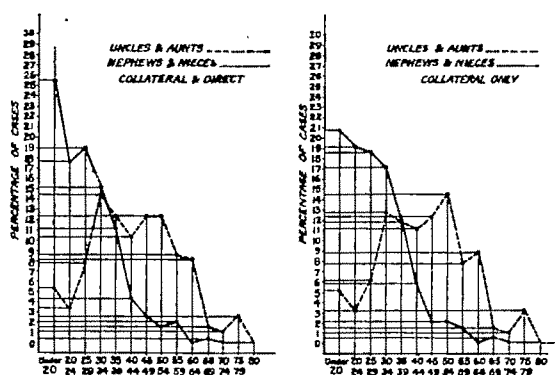


FIG. 14.

Of the insane nieces and nephews of insane uncles and aunts, 103 out of 208, or 49.5 per cent., had their first attack at or before the age of 25 years.

Uncle—nephew or niece 51 out of 98
Aunt—nephew or niece 52 „ 115

Total 103 out of 208 = 49.5 per cent.

SOME FAMILY RECORDS SHOWING ANTICIPATION.

Father—Involutional melancholia, aged 54.

Children—

- (1) Congenital imbecile, epileptic, male.
- (2) Adolescent insanity, female, aged 23.
- (3) Paranoia, adolescent insanity, male, aged 22.

Niece—Adolescent insanity, female, aged 19.

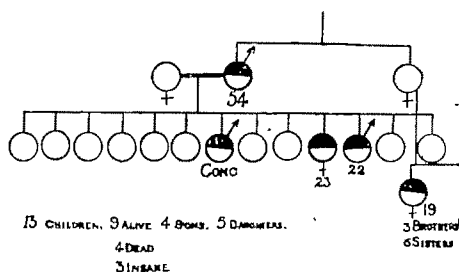


FIG. 15.

I.—*Grandfather*—Mania, recovered.

II.—*Aunt*—Alternating insanity at 45; still in asylum.

Mother—Puerperal insanity at 22; recovered.

Children—Both dementia præcox; girl discharged.

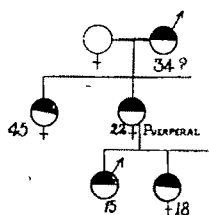


FIG. 16.

Father—Recurrent insanity, alcoholic, first attack at 46; recovered.

Children—

- (1) Girl: Recurrent insanity, aged 15; still in asylum.
- (2) Female: Recurrent insanity, aged 13; still in asylum.
- (3) Male: Recurrent insanity, aged 15; recovered.

- (4) Female: Recurrent insanity, aged 23; still in asylum.
 (5) Male: Melancholia, aged 16; died in asylum.

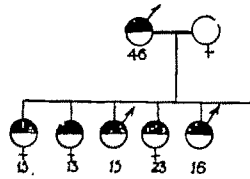


FIG. 17.

I.—*Maternal*—

Aunt—Delusional insanity (non-systematized); died in asylum.

Mother—Melancholia at 58; discharged.

Father—Recurrent insanity, aged 42; eventually died in asylum.

Children—Both adolescent insanity, and still in asylum.

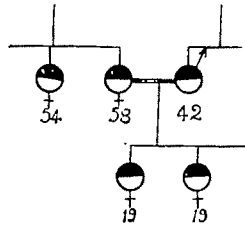


FIG. 18.

Mother—Dementia at 57; died in asylum.

Children—

- (1) Male: Recurrent insanity, two attacks; recovered.
- (2) Female: Recurrent insanity; still in asylum.
- (3) Female: Congenital imbecility; still in asylum.
- (4) Female: Congenital imbecility; still in asylum; has been in prison several times.

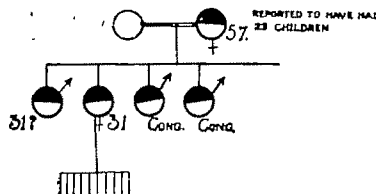


FIG. 19.

Grandfather, Paternal—"Died an imbecile."

Paternal Aunt—Recurrent insanity, aged 31; died in asylum.

Paternal Uncle—Recurrent insanity, aged 45; died in asylum.

Children—

(1) Male: Recurrent insanity, aged 19; still in asylum.

(2) Male: Dementia, aged 32; still in asylum.

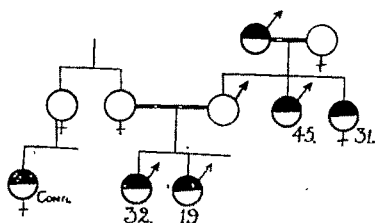


FIG. 20.

CONCLUSIONS AND INFERENCES.

What conclusions may be drawn from these collective statistics and curves which I have shown you in respect to transmission and anticipation?

First, I should remark that there are more women in asylums than men; there are about three times as many male general paralytics as female, and that about 1 to 4 of the deaths occurring in asylums are from general paralysis. Therefore the number of paralytics in an asylum is not a measure of the numbers that would occur in a card system of relatives who are at present, or who have been, in the asylums, because the average duration of life after the onset is comparatively short; nevertheless the number of general paralytics occurring among these relatives is comparatively small. This is really what we should expect if we consider this disease to be due essentially to the acquirement of syphilis and not an inborn taint of a stock. Yet probably an insane predisposition or a neurotic temperament would make a syphilitic subject more liable to the disease.

It will be observed from the accompanying tables that females more often occur among the relatives than males, the proportion being much larger than exists between male and female inmates of asylums, which is about 11 to 9. In the offspring of insane parents, daughters are much more numerous than sons—viz., in the proportion of 292 to 208. These figures show that the female sex in a stock is more liable to become insane. The figures do not seem to show that

the mother is more liable to transmit than the father, for the pairs of mother and son to father and son bear the proportion of 67 to 51, which could be accounted for by the fact that the female sex is more liable to become insane.

Next, let us see what the tables show as regards the age-periods of first attack in parent and offspring. I may here remark that congenital imbeciles are not sent to the London County Asylums unless for some special reason, and then not until they are past puberty, as a rule, so that I had to include, under 20, imbeciles and cases of early adolescent insanity. Whether we look at the tables and curves in which the number of cases form the ordinates and the age-periods the abscissæ, or the tables and curves compiled from the similar 217 pairs of father and offspring and 291 pairs of mother and offspring, in which the percentage of cases whose first attack occurred within the given age-periods are the ordinates, it is obvious that the great majority of the offspring are affected at a much earlier age than the parents; that is, there is anticipation or antedating. Whereas the great bulk of the offspring are either affected at birth or in adolescence (62 per cent. are under 30), by far the greater incidence in the parents is in the involutional period (45 to 60).

The female curves of the offspring do not quite coincide with the male, but there is less divergence than between the parents. I will endeavour to offer some explanation of these facts. There is a steady increase of the mothers at each period from 20 onwards to 60; this corresponds at first to the child-bearing period, especially 20 to 30; here there is a marked difference in the percentage between mothers and fathers; after this up to 40 the percentage of fathers predominates, although the female curve is steadily rising. I think the steady rise of the female curve is due to puerperal insanity; the increase of the males between 30 and 40, shown by a peak in the curve, is probably occasioned by a preponderance of the few relatively male general paralytics.

In conformity with the results of direct heredity in parents and offspring are the results obtained by the comparison of the tables and the curves of collateral relationship—viz., uncles and aunts and nephews and nieces. It will be observed that the same general results of the age-incidence of the two generations are shown, although there are some striking differences. If a comparison be made of the curves when there is collateral relationship only, with that of parent and offspring, it will be noticed that there is, as we should expect, a larger number of uncles or aunts in the earlier periods, and rather fewer of

nephews and nieces than in the case of direct heredity. But when we add those instances where there is direct as well as collateral insanity by including the offspring of insane parents with uncle or aunt insane, then with this more intense form of heredity added we find a larger proportion of nephews and nieces become insane in adolescence. This is shown by a higher peak in the curve at an earlier period.

I have not enough records of grandparents to draw any reliable conclusions as yet. I do not mean to affirm that there may not be some errors in the data upon which these collective statistical investigations have been made, but I think that such a simple fact as age on first attack, involving as it does no personal equation on the part of the medical men, affords a useful basis for reliable statistics. I admit that admission to an asylum may not really be the first attack either in parents or offspring or collaterals in a number of cases, but when dealing with the poor who are unable to keep an insane relative in their home, and taking into consideration the large number of cases and the systematic plan adopted, I think the facts are sufficient to prove that the Law of Anticipation is one method by which Nature seeks to either end or mend a degenerate stock.

I have not yet a sufficient collection of facts regarding the proportion of offspring born of an insane parent that become insane, but without precise data, and, from a study of a number of pedigrees, I should say that it is about 1 in 4 or 5; if, however, the ancestral stocks on both sides are tainted, it is more than this.

These curves and figures seem to show that if the offspring of an insane parent passes adolescence he has a very good chance of not inheriting the taint. Are we justified in supposing that anticipation can purify a stock? That is to say, if one or more are insane at an early period of life, will the others that are sane transmit to their offspring? That is to say, is there any probability that if these members marry into *sound* stocks the inheritance will be sound? In other words, is my hypothesis of anticipation as a coalescence of the unsound germinal elements with gametic segregation of them, leaving the other gametes free or relatively free, in accordance with facts? Or is anticipation to be explained by the fact that the germ-cell from which the insane offspring has developed is as old as the body-cells of the parent, and therefore has been subjected to the same biochemical influences? Further work is in progress to show what proportion of offspring become insane with direct and collateral heredity and convergent heredity; also what relation there is between the birth of offspring that become insane

with the attack of insanity of the parent. Some interesting facts have also been made out regarding similarity of inheritance and the influence of race, which may be summarized as follows:—

TENDENCY TO INHERITANCE OF THE SAME TYPE OF INSANITY.

Dr. Edgar Schuster has made a biometric investigation of the above material, and his results have been published in the Annual Report of the Asylums Committee for the year ending March 31, 1910. His conclusions are as follows:—

(1) A periodically insane son or daughter is more likely to be associated with a periodically insane mother or father than with one differently affected, and in the case of two offspring being insane there is even a greater tendency for a periodically insane male or female to be associated with a periodically insane brother or sister than with one differently affected.

(2) In the case of delusional insanity the tendency for the affection to run in families is very strongly marked, and the correlation between the members of the same co-fraternity is more strongly marked than between parents and offspring.

(3) In the incidence of primary dementia of adolescence there is a strong correlation between members of the same co-fraternity; there is also a decided tendency indicated for the brothers and sisters of imbeciles to be also imbeciles.

(4) There is no indication of general paralysis running in families. This is not surprising, as it is now recognized to be an acquired disease due to syphilitic infection.

Racial Inheritance.

It has always struck me that Jews were, on account of their neurotic temperament, more liable to insanity than Christians. The following statistics seem to support this inference.

All the insane Jews are admitted to Colney Hatch Asylum. The number of cards belonging to Jews in this asylum is 80; the number belonging to the non-Jewish inmates is 254. The total number of inmates is 2,450, and of these 459 are Jews, so that less than one-fifth of the total population is Jewish. A little more than one-fourth of the relative cards belong to Jews, so that the incidence of ascertained relationship among the Jewish inmates is considerably more than among the non-Jewish. No doubt the temperament of the Jews renders them as a race more liable to the neuropathic tendency, but the greater

incidence of ascertained relationship among the Jews is partly due to the following facts: They are more often visited by their friends, they have more pride of family, and as a rule are more intelligent and anxious to afford information. But to counterbalance this it must be remembered that the greater number of these Jews are aliens who have come from Russia and know nothing about the relatives who may be there, or who have emigrated to the United States. Probably, therefore, this rather under-estimates than over-estimates the proportion of Jews with insane relatives as compared with Christians.

Maudsley in his philosophical work on "The Pathology of Mind," a book in my opinion now far too little read, says: "There appears to be at work a silent tendency in Nature to restore an insane stock to a sound type if regeneration be possible, or to end it if its degeneration be such that it is too bad to mend." This conclusion, which he has arrived at from a wide experience and knowledge combined with philosophical deduction, seems to be proved by the facts which I have brought to your notice.

Finally, it may be asked, if Nature is continually purifying stocks, how comes the pollution? All biologists, even those who do not believe in the transmission of acquired characters in the Lamarckian sense, admit that nutritional conditions may be a source of variations occurring in the germ-plasm. The germ-cells are nourished by the same blood and lymph as the body-cells, and prolonged changes in the blood caused by poisons introduced into the body may induce permanent biochemical alteration in the blood and lymph, which would therefore be capable of affecting the germ-cells, especially during maturation. Thus syphilis, alcohol and tuberculosis may modify the nutrition and cause pathological variations in the germinal determinants of the latest acquired structure of the body—viz., the cortical neurones—not necessarily affecting them structurally, but only nutritionally and in their specific vitality, causing a tendency to an unstable nervous condition which may be the starting point of degeneracy of a stock, especially when added factors occur, such as the strife of city life with its feverish pursuit of gain and pleasure, competitive examinations, the constantly increasing departure from simple modes of life, the unphysiological conditions of sexual life, and the extension of more refined physical and mental enjoyments, bringing with them desires and emotions previously unknown.

SENSORY DISTURBANCES FROM CEREBRAL LESIONS.¹

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¹ The substance of this paper formed the Croonian Lectures delivered before the Royal College of Physicians on June 13, 15, 20 and 27, 1911.

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WE must begin by craving the indulgence of our readers for the form in which the following paper is cast. The nature of the sensory changes produced by lesions of the cerebral cortex and other parts of the brain has been the theme of innumerable works by the acutest intellects in medicine of the last fifty years. Our research would have been impossible but for their labours, and yet we can never acknowledge what we owe to them. Many, whose views have helped to make our work fruitful, are known to us through their publications, and to them we can repay our debt by referring at suitable points to the similarity of our results to those of our predecessors.

Others have been our teachers and the masters for whom we have gladly worked. To them our debt can never be repaid, for much of the identity in outlook comes from personal intercourse and cannot be fixed by citation. First amongst this group must always stand the name of Dr. Hughlings Jackson.

This paper is a preliminary communication in which we put forward a general view of the mode of action on the afferent side of the nervous

system. Any such generalization must not only contain much that is common to the views of others, but also many things incompatible with the conceptions, even of those with whom we are otherwise in harmony. Where possible, we shall always acknowledge our concurrence with those who have preceded us, but in the small space at our disposal we cannot enter into criticism of work with which we are not in agreement. In many cases, although our theoretical conclusions may coincide with those put forward by other workers, our experimental results may differ fundamentally. In the same way, similar clinical observations may lead us to other conclusions, but it will be impossible to stop our exposition in order to discuss these differences.

We shall attempt to put forward in this paper a general conception of the mechanism underlying sensation, based upon a study of human beings in whom disease, accident, or surgical interference has produced some stationary lesion. Many of these patients have occupied our attention from time to time for many years, and it will be impossible in this preliminary communication to give a complete history of all our cases. We have, however, added in an appendix an abbreviated account of the physical signs of certain patients, to which we shall frequently allude for the sake of illustration.

We lay great stress upon the methods we have used for testing sensibility in this research and have therefore detailed them fully in another appendix to this paper. Here we have described the difficulties which may arise and the means we have taken to overcome them. As far as possible we shall avoid the use of all general terms. We wish to lay peculiar stress on the confusion which arises from the use of all such expressions as "deep sensibility," when reporting the results of a clinical examination; not infrequently, "deep sensibility" is said to be affected from a lesion of the cortex, when the observer means to state that the appreciation of posture, of passive movement, or of vibration, is defective. Similarly, "atopognosis" is a combined loss of the faculties of recognizing position in space and the situation of the spot stimulated, two functions capable of independent investigation. In every case, therefore, we shall describe our observations under headings which imply the simple test used in analysing the loss of sensation.

Cases of disease may be studied from two aspects. More commonly, it is our business as physicians to consider their relation to clinical types, and to discuss the diagnostic significance of certain signs and symptoms. But, in this paper, disease is simply the means by which certain laws are demonstrated and certain physiological activities are

laid bare. It is not the disease which occupies our attention, but the opportunities it gives for analysing the processes underlying sensation. We shall therefore begin by tracing sensory impulses from the point where they enter the spinal cord, and follow them to those centres where they form the basis of that psychical process we call sensation.

For this investigation, exact knowledge of the site of the lesion is less important than a precise determination in selected cases of the nature of the sensory changes. We are occupied in this research with certain forms of sensory loss and with certain dissociations of sensibility; our aim is to discover the grouping of afferent impulses at different levels of the nervous system and not to determine the regional diagnosis of organic lesions. The most definite sensory grouping and dissociation are exhibited in cases where the lesion is stationary and the patient otherwise in perfect health, whilst in many instances where the lesion could be determined *post-mortem* the patient was entirely unsuitable for sensory examination. It is only by the exact study of these affections of sensation that we can obtain any knowledge of the nature of cerebral activity and of the form in which impulses reach the higher centres to underlie the production of sensation.

It is our pleasant duty to express our sincere thanks to all those who have helped us in this work. To the staff of the National Hospital, Queen Square, we owe innumerable opportunities of observing many valuable cases, and Dr. Head wishes to thank them for their generous hospitality. To Sir Victor Horsley we are particularly grateful for permission to use our observations on his remarkable case of excision of a portion of the cerebral cortex.

In consequence of such help we have been able to investigate a large number of selected cases. This includes twenty-four patients in whom the clinical symptoms justified us in assuming certain affections of the optic thalamus. A second group consists of sixteen patients with limited lesions of the surface of the brain, most of which resulted from successful removal of a cerebral tumour or other cortical disease. In this group, the site of the lesion is known with more or less accuracy, and we have included solely stationary cases examined months or years after operation. We have also examined the effects produced upon sensation by acute destructive lesions and advancing cerebral tumours; in this way we have studied the effects of the condition called by Monakow "diaschisis." Finally, we have employed the same methods to investigate many instances of disease in the neighbourhood of the internal capsule and deeper parts of the brain.

CHAPTER I.—THE GROUPING OF AFFERENT IMPULSES IN THE
SPINAL CORD AND BRAIN-STEM.

§ 1.—*The Spinal Cord.*

It is a matter of universal belief that man has been evolved from the lower animals; and yet, when we deal with sensation and sensory processes, we speak as if he were created with peripheral end-organs, each capable of reacting to one of the sensory qualities of human experience. The impulses starting in these end-organs are supposed to pass unaltered to the brain, there to set up that peculiar and unknown change which underlies a specific sensation.

Spots were found on the skin sensitive to touch, to pain, to heat or to cold only. With the discovery of these highly developed end-organs, the doctrine of specific nerve-energy seemed to be proved in the strictest manner. All other forms of sensory appreciation were supposed to be produced by the psychical transformation of these primitive sensory elements, in association with an ill-defined faculty called the "muscle-sense." Recognition of the locality of a stimulus and the posture of the limbs were attributed to judgment and association.

But alongside the systematic investigation by von Frey and others of the capabilities of these specific areas in the skin, the clinicians were discovering the importance of "muscular sensibility." Sherrington's demonstration of afferent fibres in muscles and tendons placed the existence of the "muscle-sense" beyond a doubt, and the use he made of these afferent impulses from deep structures, in his theory of the proprioceptive system, necessitated a complete exploration of the nature of deep sensibility.

By their experiment directed to this end, Rivers and Head [33] showed that beneath the skin, independent of all "touch-" and "pain-spots," lies an afferent system capable of a wide range of functions. Pressure, that in ordinary life would be called a touch, can be appreciated and localized with considerable accuracy. Increase of pressure, especially on bones and tendons, will cause pain. Moreover, it is from the impulses of this deep afferent system that we gain our knowledge of the posture of the limbs and the power of recognizing passive movements.

Evidently, therefore, the peripheral mechanism of sensation is less simple than was at first supposed. For there are two sets of end-organs, that can respond to tactile stimuli, and two independent mechanisms for the initiation of pain. Further analysis showed that the peripheral apparatus in the skin, by which we become conscious of the nature of

external stimuli, is highly complex. No one sensory quality is subserved by a single set of end-organs, but every specific sensation is the result of the combined activity of more than one group. This is exactly the result that might have been expected, when we bear in mind that, the structure of man is the product of a long evolution.

But it is equally obvious, from an evolutionary standpoint, that these diverse impulses could not pass uncombined to the highest physiological level. Within the spinal cord, the opportunist grouping of the periphery gives place to an arrangement according to quality (Head and Thompson [12]). All impulses capable of generating pain become grouped together in the same path, and can be disturbed simultaneously by an appropriate lesion of the spinal cord. In the same way, sensibility to heat or to cold may be lost independently of one another, showing that all the impulses upon which they are based have been sorted out into two functional groups, each of which passes by a separate system in the spinal cord.

The most remarkable condition revealed by an intramedullary lesion is the complete separation of the impulses underlying the appreciation of posture, the discrimination of two points and their correlated faculties from those of other sensory groups. All painful and thermal impulses, coming from the periphery, undergo regrouping after entering the spinal cord, and, whether they arise in the skin or in deeper structures, become arranged according to functional similarity. Then, after a longer or shorter course, they pass away to the opposite side of the spinal cord.¹

This process of filtration leaves all the impulses associated with postural and spacial recognition to continue their course unaltered in the posterior columns; they are the survivors of peripheral groups broken up by the passing away of certain components into secondary afferent systems. At any point in the spinal cord, these columns transmit not only impulses from the periphery which are on their way, after a longer or shorter passage, to regrouping and transformation, but at the same time they form the path for impulses, arising both in the cutaneous and deep afferent systems, which undergo no regrouping until they reach the nuclei of the medulla oblongata.

Thus, a lesion confined to one half of the spinal cord, even at its highest segment, may interfere with the passage of sensory impulses,

¹ Tactile impulses seem to run in two paths: one in the same half of the spinal cord to that by which they entered, the other on the opposite side of the spinal cord (Petrén [28, '30], Head and Thompson [12]).

some of which are travelling in secondary paths, whilst others are still within the primary level of the nervous system. All impulses concerned with painful and thermal sensations from distant parts, disturbed by such a lesion, will be travelling in secondary paths and will have come from the opposite half of the body; for, after regrouping, they have passed across the spinal cord. But those impulses underlying the appreciation of posture, the compass-test, size, shape, form, weight, consistence and vibration will be affected on the same half of the body as the lesion. They still remain in paths of the peripheral level and have undergone no regrouping.

In such a case the parts on the side opposed to the lesion may be insensitive to pain, heat and cold; but all the postural and spacial aspects of sensation will be perfectly maintained. Yet, all power of recognizing position, of estimating size, shape, form and weight, or of discriminating the two compass-points, will be lost in the limbs which lie on the side of the lesion, although tactile sensibility and localization of the spot stimulated may be perfectly preserved.

This remarkable arrangement enables us to analyse the nature of the peripheral impulses upon which depend our power of postural and spacial recognition. Obviously, even at the periphery, they must be independent of touch and pressure. The power to distinguish two points applied simultaneously and to recognize size and shape requires as a preliminary the existence of sensations of touch; but the patient may be deprived of all such powers of spacial recognition without any discoverable loss of tactile sensibility. In the same way our power to appreciate the position of a limb, or to estimate the weight of an object, is based upon impulses which, even at the periphery, exist apart from those of touch and pressure called into simultaneous being by the same external stimulus.

This long delay of the postural and spacial elements in reaching secondary paths enables them to give off afferent impulses into the spinal and cerebellar co-ordinating mechanisms, which lie in the same half of the spinal cord. The impulses which pass away in this direction are never destined to enter consciousness directly. They influence co-ordination, unconscious posture and muscular tone, and, although arising from the same afferent end-organs, they never become the basis of a sensation.

Finally, the last survivors of these impulses from the periphery become regrouped in the nuclei of the posterior columns and cross to the opposite half of the medulla oblongata in paths of the secondary level.

So they pass to the optic thalamus and thence to the cortex, to underlie those sensations upon which are based the recognition of posture and spacial discrimination.

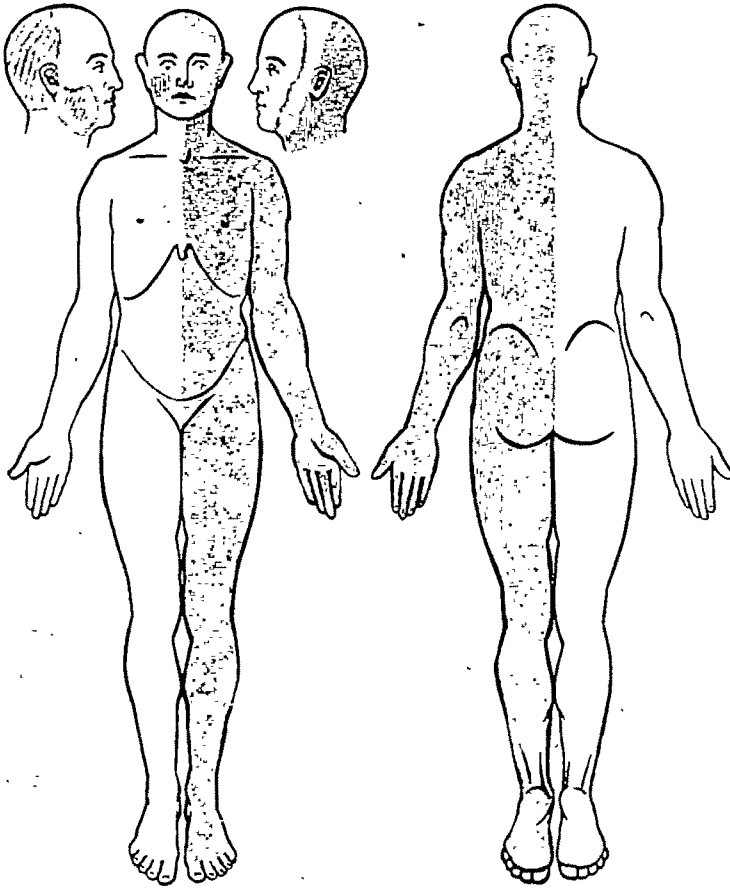


FIG. 1.—To show the loss of sensation in Case 1. The shaded area on the right half of the face corresponds to the parts over which sensibility was diminished or lost to prick. Over the left half of the body the dark parts were insensitive to prick, heat and cold. Over the left arm and leg, pressures of 15 to 18 kg. on the pressure-algometer produced no pain.

The following case is an example of the effects produced by a lesion situated in one half of the spinal cord just below the point at which the postural and spacial impulses become regrouped in the nuclei of the posterior columns.

CASE 1.—*Brown-Séquard paralysis.**On the Right—**Weakness of arm and leg.**Reflexes exaggerated; ankle-clonus and extensor plantar reflex.**Loss of painful sensibility over right cheek (fig. 1), though touch, heat and cold were unaffected.**On the body and limbs, tactile, painful and thermal sensibility were perfect; but in the right arm and leg, posture, passive movements and vibration of a tuning-fork could not be appreciated within normal limits, the compass-test was defective, and he could not recognize size, shape, form, weight, or consistence of objects in the right hand.**Localization was not affected.**On the Left—**Motion perfect.**Reflexes normal.**Loss of sensation to pain, heat and cold as in fig. 1.**All other forms of sensibility, including localization, perfectly preserved.*

W. C.,¹ a man, aged 34, was in perfect health until he was thrown from his van in consequence of a collision on May 30, 1908. He was concussed and did not regain consciousness until three weeks after his accident, when he found he was unable to move his right arm and leg. Speech was in no way affected and movements of his face were never impaired. Slowly he regained power over the right arm and leg, and about two months after the accident he was able to walk. From the first he knew he could not recognize the position of the right arm, but was unconscious of the loss of painful and thermal sensibility on the left half of the body.

When we first examined him nearly two years later (February, 1910), all movements of his right arm could be performed within a normal range, but they were distinctly weaker than those of the opposite side. The tone of the muscles of the right upper extremity was increased, but there were no organic contractures.

His gait showed a certain awkwardness, but he did not drag the right foot. All movements could be readily carried out, although his strength was slightly less in the right than in the left lower extremity. The tone of the muscles of the right leg was not increased.

All reflexes on the left half of the body were normal, but the arm-, knee- and ankle-jerks on the right side were much exaggerated and the plantar reflex gave an extensor response. Slight clonus was obtained at the right ankle.

Ocular movements and the reactions of the pupil were in no way affected, and the face, tongue, and palate moved equally on the two sides. But on the right cheek and in the occipital region sensation was disturbed (fig. 1). Over the greater part of this area, the patient was insensitive to a prick, but the borders were not sharply defined, merging gradually into

¹ We owe the opportunity of examining this man to the kindness of Dr. James Collier.

parts of normal sensibility. Over the occipital region 15 kg. of pressure, applied with the algometer, produced no pain, whereas on the left half of the skull he responded to 5 kg. Cotton-wool was appreciated everywhere; but over the central parts of the area; on the right cheek and ear, the tickling sensation, easily evoked from the left half of the face, was absent. The patient recognized the touch of a hair of 21 grm./mm.² within the affected area, and no difference could be discovered between the two halves of the face to measured tactile stimuli. Sensibility to heat and cold was not disturbed, the compass-points were readily distinguished at 2.5 cm., and localization was perfect.

This loss of sensation on the right half of the head formed the local manifestation of a lesion situated in the right half of the spinal cord. As in most Brown-Séquard paralyses, the remote effects of this destruction appeared as a loss of sensation to painful and thermal stimuli on the opposite (left) half of the body. This loss was absolute to every form of pain and to all degrees of temperature over the area shown in fig. 1. Not only was the patient insensitive to prick, but pressures of from 15 to 18 kg. produced no pain over the left arm or leg. All forms of tactile sensibility were, however, completely preserved. The compass-points could be accurately distinguished and localization was perfect. The position of all portions of the left arm and leg were recognized with ease, and passive movements were appreciated within normal limits.

When we turn to the condition of the right half of the body, that is, to the parts on the side of the lesion, we find almost the exact converse. All sensibility to touch, pain and temperature was perfectly preserved, but the patient was unable to recognize the posture of his right arm and leg, and could neither name nor imitate correctly the position into which they had been placed. Movements made passively were not recognized, until they exceeded from five to eight times the normal range.

Thus, for instance, movements of the index-finger on the right and left hands, which could be appreciated subtended the following angles measured in degrees:—

Left	Flexion	$2\frac{1}{2}$ 2 $2\frac{1}{2}$ 2. $2\frac{1}{2}$				
	Extension	3	$2\frac{1}{2}$	$2\frac{1}{2}$	$2\frac{1}{2}$	$2\frac{1}{2}$
Right	Flexion	15	15	$17x$	$15x$	$22x$
	Extension	17	17	$30x$	27	28

But, although movements of the right index were appreciated, when the finger had been moved through the number of degrees on this formula, the direction of movement was wrongly given in those cases where an x is added to the figure.

The vibrations of a tuning-fork were appreciated badly or not at all over the right arm and leg, in spite of the complete integrity of tactile and pressure sensibility, and the compass-points were not perfectly distinguished on the right palm, even at a distance of 6 cm. from one another. On the left palm a perfect reading was obtained at 2 cm.

All power of recognizing size, shape and form in three dimensions was absent in the right hand, in spite of the existence of perfect tactile sensibility.

The power of estimating weight and the relative amount of pressure exerted by two otherwise similar objects was lost on the right hand. Moreover, the patient was unable to recognize the difference between even the hardest and the softest of the objects used to test consistence, when they were compressed between the fingers and thumb of his right hand.

And yet, in spite of this sensory disturbance localization was perfect in the limbs of the right half of the body, and the two points of the compasses, if applied to the skin one after the other, were perfectly appreciated on the two hands.

This case is an excellent illustration of the principles laid down in this section, and the retention of muscular power in the right hand enabled us to test the faculty of recognizing size, shape, form in three dimensions, weight and consistence with an accuracy otherwise impossible.

In conclusion, we believe that at the extreme upper end of the spinal cord, just below the formation of the posterior column nuclei, afferent impulses pass upwards in three main divisions :—

(1) The impulses underlying sensations of pain, of heat and of cold are travelling in secondary paths, in the opposite half of the spinal cord from that by which they entered.

(2) Those impulses, upon which depend postural recognition and spacial discrimination still remain uncrossed in the posterior column. They consist of one group, arising in the deep afferent system, upon which depend our recognition of posture, passive movement, weight, consistence and vibration. A second group arises in the end-organs of the skin and these impulses underlie the discrimination of two points applied simultaneously, and the allied appreciation of size, shape and form in three dimensions.

(3) Contact sensibility evoked by touch and by pressure may remain entirely undisturbed. Apparently it depends upon impulses which run in a double path and it is therefore unaffected by a purely unilateral lesion (Rothmann [34], Petré [28], Head and Thompson [12]). This tactile group, formed by the union of tactile impulses within the cord, carries with it the impulses which underlie the power of recognizing with accuracy the situation of the stimulated spot, and localization therefore remains unaffected.

§ 2.—*The Brain-stem.*

The larger number of afferent impulses traverse the spinal cord, grouped, according to their sensory qualities, in paths that can be isolated by disease. This enables us to analyse the nature of the groups

formed, either by specific selection at the first synaptic junction, or by gradual filtration away into secondary tracts, of impulses arising originally in the same peripheral system. But, in their further passage through the brain-stem to the optic thalamus, the impulses run in paths which are anatomically more closely associated. This makes any analysis of the grouping of afferent impulses in this region unusually difficult.

Impulses underlying sensations of pain, heat and cold seem alone to run unaltered between the upper end of the spinal cord and the optic thalamus.¹ They receive the accession of the regrouped secondary impulses from the face, which cross to join the specific paths for pain, for heat or for cold. These paths are so situated that they can be interrupted without disturbance of any other form of sensation on the body, and the analgesia and thermo-anæsthesia so produced resemble in quality the loss to pain, heat and cold caused by a lesion of the spinal cord.

Thus, when a lesion of the bulb interferes with sensations of pain, not only may the skin be insensitive to prick but the readings of the pressure-algometer may be raised on the analgesic side. In the same way, the affected area on the body may be insensitive to all degrees of heat and to all stimuli capable of evoking normally a sensation of cold.

It is, however, important to remember that although the uncomfortable sensation produced by excessive pressure is greatly diminished, a lesion in this situation does not usually abolish completely all painful pressure (Case 2, Case 3). Thus it would seem that the grosser forms of pain and discomfort may possibly find their way by another path, if the usual one is closed; whereas, an equivalent lesion in the spinal cord blocks all painful impulses whatever their origin.

Not only can these three forms of sensibility be affected together, but any one of them may escape or be affected alone. Thus von Monakow [26] described loss of sensation to heat and cold without analgesia, and in the case recorded by Mann [22] and later by Kutner and Kramer [19] sensibility was lost to pain and to heat, whilst that to cold was unaffected (cf. also Wallenberg [41] and Marburg [23]).

The following case shows that, with a lesion of the bulb, the opposite half of the body may become analgesic and yet the threshold-values of sensibility to heat and cold may be equal on the two sides.

¹ This does not necessarily mean that the impulses are carried by uninterrupted fibres. It has been suggested by Long [20], Cajal [4], Kohnstamm [17], that the nuclei of the formatio reticularis are intercalated in the course of the afferent conduction tracts. Such anatomical relay would not interfere with the above physiological conclusions, as it does not necessarily imply any regrouping of sensory impulses.

CASE 2.—October, 1906, sudden onset of pain in the right lower jaw. Since June, 1907, he has noticed loss of sensation on the left half of the body and right half of the face. First seen by us June, 1909, and since then his condition has not changed materially.

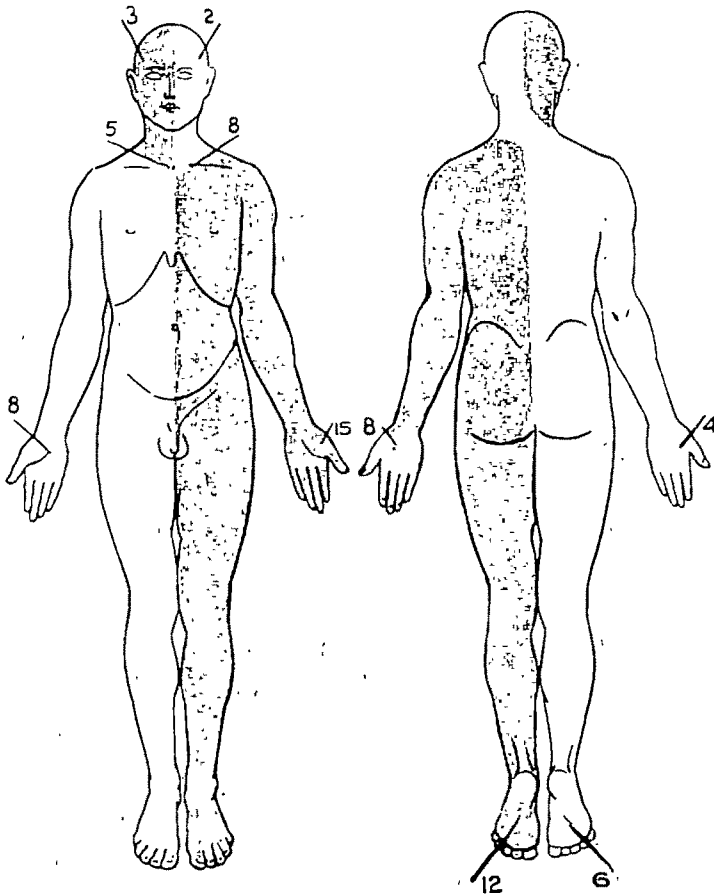


FIG. 2.—To show the loss of sensation in Case 2. The right half of the face was analgesic to prick, but pressure-pain was not lost. The left half of the body was insensitive to prick, and the readings of the pressure-algometer were uniformly higher than over similar parts on the normal side.

Motor power and reflexes unaffected.

Diplopia in all directions. Pupils unaffected. Optic neuritis in both eyes. Hearing diminished in right ear.

Sensation on the face.—Loss to prick with no loss to pressure-pain over the area in fig. 2. No other change in sensation to measured stimuli, but touch

seemed "less vivid," heat "hotter," and cold "less cold," over right than left half of the face.

Sensation on the body.—The left half, except the perineum and scrotum, was insensible to prick (fig. 2). Pressure-pain was also diminished. Otherwise sensation was unaffected.

F. C. F., aged 34. (This patient was first seen by us when he was in the National Hospital, under the care of Sir William Gowers, in June, 1909.) He was a teetotaler, a married man, and denied all venereal disease.

In October, 1906, pain came on suddenly in the right lower jaw as he was sitting in the barber's chair. He became pale and faint and "felt queer" for the rest of the day. The pain continued unaltered until May, 1907, when it grew more severe and reached its height in June of the same year. In the following nine months it gradually diminished, but returned in April, 1909:

A sharp, stabbing headache in the occipital region first appeared in September, 1907. This has slowly increased in severity. Vomiting began in July, 1907, and has continued on and off ever since.

He has noticed some disturbance of sensation on the left half of the body and right half of the face since June, 1907.

He has not been definitely giddy, but occasionally sways when walking on the pavement.

In June, 1909, motion was not affected,¹ and the reflexes did not differ materially on the two halves of the body.

He complained of diplopia in all directions, greater on looking upwards, when the images were crossed; with movements to the right or to the left they were uncrossed. The pupils reacted well and were central in position. Movements of his jaw, face, palate and tongue were carried out perfectly on both sides.

Smell was not affected; but the ammonia reflex was almost completely abolished from the right nostril. Taste was lost on the right half of the outstretched tongue. Hearing was slightly diminished in the right ear compared with the left; the tuning-fork placed on the forehead was not heard on the right side. The fields of vision were normal and there was no colour loss; but optic neuritis was visible in both eyes, more evident in the right. The discs were pale and the cup filled up.

Sensation on the face.—He complained of occasional spasms of pain in the right half of the face, closely resembling those of tic douloureux. No difference between the sensibility of the two sides could be discovered with cotton-wool, von Frey's hairs, Graham-Brown's aesthesiometer, or to the compass-test and vibration, but he complained that all forms of touch were "less vivid" over the right than over the left half.

The whole of the area shown on fig. 2, together with the right half of the tongue, was, however, insensitive to prick; though the algometer gave approximately equal readings on the two sides.

Both heat and cold were appreciated on the two halves of the face, but

¹ For co-ordination *vide infra*.

although the thresholds were the same, all heat seemed hotter over the affected half, while cold stimuli seemed colder over the normal parts of the face.

Sensation on the body.—Localization, the compass-records, the appreciation of size, shape, form and weight, were equally good on the two halves of the body.

Cotton-wool was recognized everywhere, and the same measured tactile stimulus was required to produce a sensation of contact on the two halves of the body. There was no difference in the threshold for the appreciation of roughness and the length of time during which vibration could be recognized; but both sensations of touch and vibration were more vivid on the normal than on the left half of the body.

Heat and cold could be appreciated everywhere, but all degrees of warmth seemed hotter over the affected half of the body (left). Any cold stimulus, on the other hand, seemed colder over normal parts.

The whole of the area (fig. 2) shown on the left half of the body was insensitive to prick; but it will be seen that a small area in the left perineum and the greater part of the penis and scrotum of the same side responded to the prick of a pin. The left testicle was, however, entirely insensitive to pressure, whereas the normally unpleasant sensation could be easily evoked from that of the right side. The pressure of the algometer, necessary to evoke pain, was considerably higher on the left than on the right half of the body (fig. 2), especially on the palms and on the soles.

The position of the limbs was recognized as well on the one side as on the other, and passive movements of all the joints were perfectly appreciated. And yet in spite of perfect recognition of posture and movement, there was distinct inco-ordination of the left hand. He knew that the movement was not absolutely correct; thus, if asked to touch a spot on a sheet of paper with his eyes closed, the left index-finger deviated to a much greater extent than the right. But so sure was he of the position of the affected hand that he could place the normal forefinger accurately upon the wandering left index without opening his eyes.

Thus this case showed (1) a local lesion affecting the sensation of the right half of the face and neck; (2) a remote disturbance of sensibility to pain over the left half of the body with considerable raising of the algometer readings over the analgesic area; (3) with heat and cold the same threshold was obtained on the two halves of the body.

All recent work has shown that the paths for the transmission of the impulses for pain, heat and cold run up in the neighbourhood of the nucleus of the trigeminal nerve. This close local association is particularly well shown by cases of occlusion of the posterior inferior cerebellar artery (Wallenberg [40], Breuer and Marburg [2], Spiller [39]).

In addition to these well-known facts, the following instance of this condition also shows that impulses underlying the appreciation of

posture and passive movement have become separated from those concerned with spacial discrimination. The compass-test gave identical results on the two halves of the body, and size, shape and form in three dimensions could be appreciated on both hands. And yet the amount of passive movement necessary to evoke a sensation was three to four times greater in the affected fingers. Evidently, a change in grouping has taken place at the posterior column nuclei and the impulses for spacial discrimination now tend to run apart from those of postural recognition.

CASE 3.—*An instance of "occlusion of the posterior inferior cerebellar artery." Sudden onset December 25, 1908. Seen by us first in July, 1909.*

Horizontal and rotatory nystagmus, but diplopia had passed off. Left pupil did not dilate fully to shade. Left palpebral fissure smaller than right. Movement of left half of the palate defective, but vocal cords and tongue moved well.

Gait unsteady: he tended to deviate to the left but fell to the right when his eyes were closed. No paralysis.

Reflexes normal.

Sensation on the face.—Left half insensitive to prick, but sensitive to pressure-pain (fig. 3). Tactile and thermal thresholds were equal and normal on the two halves of the face, but all temperatures seemed "duller" on the left half.

Sensation on the body.—Loss to prick, to heat and to cold over the right half of the body, right arm and right leg (fig. 3). Sensibility to pressure-pain diminished over this area but not lost.

Diminished power of recognizing posture and passive movement in right arm and right leg.

All other forms of sensation normal.

W. S., a man, aged 50, suddenly fell upon the floor just as he had finished breakfast on Christmas morning, 1908. He was not unconscious but intensely giddy. On trying to rise he fell to the right, helpless and unable to stand. Vomiting came on at once and was almost continuous for thirty-six hours. He was put to bed, where he remained for eight weeks, compelled to lie almost constantly on his left side.

From the beginning, he complained that the right half of the body "felt cold and numb," although he could appreciate "the slightest touch" and knew where his limbs lay in bed. He could always move the right arm freely, but was unable to use it for taking food; he said, "I could hold a spoon in my right hand, but I could not be certain of putting it properly into my mouth." In the same way he found some difficulty in directing the movements of the right leg.

When he left his bed, at the end of eight weeks, he staggered as if drunk and always felt as if he was falling towards the right. But on the other hand, when sitting in a chair he frequently seemed to be drawn over to the left. This giddiness disappeared completely in seven months and he recovered sufficient control over the right arm to return to work in July, 1909.

Immediately after the stroke he saw double; the two images appeared side by side, and he believed that the one to the left was the false one. For a time the left upper eyelid "drooped," and he found that the left cheek did not sweat and was colder when he touched it than the right. From the beginning of his

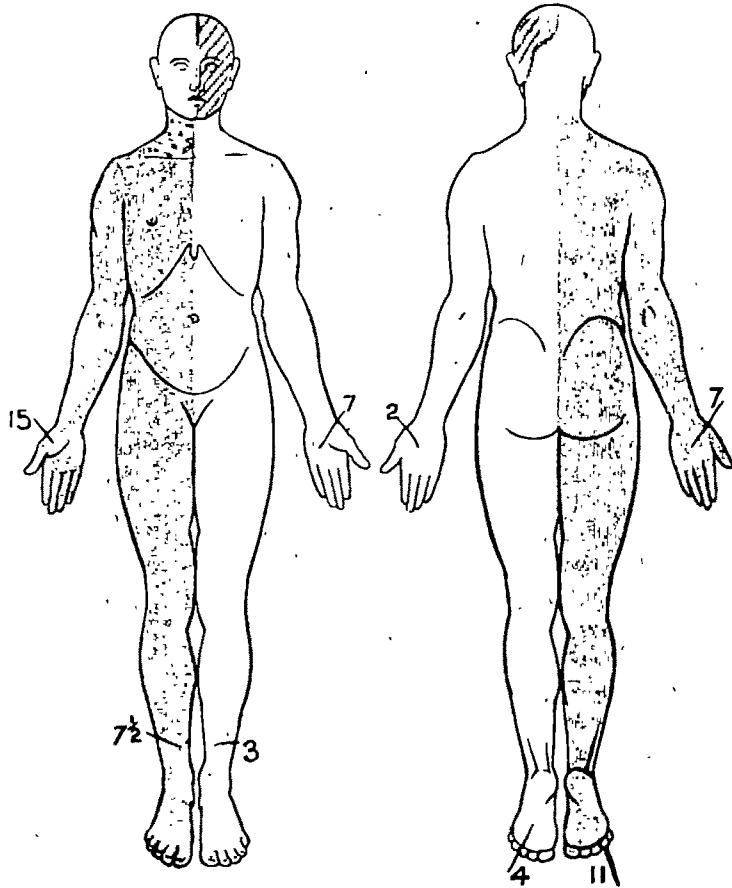


FIG. 3.—To show the loss of sensation in Case 3. The left half of the face was insensitive to prick but sensibility to pressure-pain was unaltered. Over the darkened area on the right half of the body sensations of heat, cold and pricking were abolished. Pressure-pain, though diminished, was not lost.

attack, he noticed that the left half of the face seemed numb, and this has persisted unchanged up to the present time. All food appeared to be very cold on the left half of the mouth and he lost taste on the same half of the tongue. At first he found considerable difficulty in swallowing; solid food seemed to stick in his throat. His voice became hoarse at the time of the stroke. He

was never deaf, but since the attack has suffered from tinnitus in the left ear, "like a cricket whistling."

We saw him first in July, 1909, owing to the kindness of Dr. Golla. He was an intelligent, healthy-looking man with somewhat rigid arteries. The left eye was a little more sunken and the palpebral fissure somewhat smaller than on the right side. He no longer saw double, and all ocular movements were normal in range; but, on full lateral movements, slight horizontal and rotatory nystagmus was visible, the rotation having an outward and downward direction. The left pupil was slightly smaller than the right; it reacted well to light and on accommodation, but did not dilate so rapidly and so fully as the right when shaded, or when the skin of the neck and cheek was stimulated.

The muscles of the jaw acted normally, and volitional movements of the face were equal on the two sides, but, when talking or smiling, the left half moved more than the right.

The left half of the palate was less active and the uvula was drawn definitely over to the right. The vocal cords moved well and all difficulty in swallowing had passed away. Movements of the tongue were perfect.

Taste and smell were not affected when we first saw him, but the ammonia reflex from the left nostril was certainly greatly diminished. Hearing and vision were normal.

He could walk without help, although he was evidently careful and afraid of stumbling; no difference could be discovered between the lower extremities, but he tended to keep the legs abducted and to turn the toes a little outwards in walking. Moreover, when walking quickly he deviated to the left and constantly corrected himself voluntarily. But, as soon as his eyes were closed and he was told to walk forwards, he fell to the right in consequence of the defective sense of position and movement in the right leg.

The strength of the movements and the tone of the muscles were almost equal in both arms and no difference could be discovered between the two lower extremities. The movements of the left arm were slightly ataxic, whether the eyes were open or closed. Rapidly repeated movements were equally well carried out with both upper extremities.

There was no material difference between the reflexes on the two halves of the body and both plantars gave a flexor response.

Sensation on the face.—Both halves of the face responded equally well to cotton-wool and von Frey's hairs, but the left forehead, temple and cheek were insensitive to prick (fig. 3); this area merged gradually behind into parts of normal sensibility. Over the temples and malar bones the pressure-*algometer* gave the same readings on both sides ($1\frac{1}{2}$ and 2 kg.). The left cornea was insensitive to a hair of 23 grm./mm.² and the left conjunctiva did not respond to 100 grm./mm.², whereas 8 grm./mm.² produced a quick reflex and a sensation of sharpness on the right cornea. From the normal conjunctiva 23 grm./mm.² immediately evoked an uncomfortable sensation. The threshold for the appreciation of heat and of cold was the same on the two sides, but the patient complained that all temperatures produced a

"duller" sensation on the left half of the face. Both sides responded equally well to vibration and to the compass-test.

Sensation on the body.—All forms of tactile sensibility were perfectly preserved, vibration was appreciated and localization was perfect on both sides. The compass-records were equally good from both hands and from the soles of both feet. Weight, size, shape and form were accurately recognized.

Sensibility to prick began to be defective at the line marked on fig. 3. The loss of sensation gradually deepened until on the right arm, trunk and leg it was complete. Over the whole of this half of the body, the pressure necessary to cause pain was uniformly higher than over similar parts on the other side, as shown by the numbers on fig. 3. Both testicles were sensitive, but the sensation was more uncomfortable from the left than from the right.

Over the same area on the right half of the body he was insensitive to all degrees of temperature and, although the borders of this loss of sensation corresponded to those of the analgesia, they were more definite.

The power of recognizing posture was also certainly somewhat diminished in both the right arm and the right leg. The existence of this loss was confirmed by measurement of the smallest perceptible movement. Thus extension and flexion of the index-finger of the left hand were recognized with a movement of just over 2° ; whereas on the right hand the average flexion necessary for recognition was 7° , whilst extension of over 8° was required to evoke a sensation of movement.

This typical case of "occlusion of the posterior inferior cerebellar artery" showed:—

(1) A sensory disturbance over the left half of the face representing the local lesion.

(2) Analgesia, with raising of the algometer readings, and complete loss of sensation to heat and to cold over the right half of the body.

(3) Diminished recognition of posture and passive movement in the right arm and leg, but all spacial discrimination was perfect (compass-test, appreciation of size, shape, form).

(4) Slight cerebellar inco-ordination in the left arm and leg, which was not increased by closing the eyes.

When all afferent impulses from the face have undergone regrouping and passed, in secondary tracts, to the opposite half of the nervous system, the various sensory paths are gathered closely together in preparation for their ending in the optic thalamus. Every sensory path now lies within the opposite half to that by which the impulses entered the central nervous system.

From the analytical aspect, these mid-brain lesions can give little information as to the grouping of the elements underlying sensation.

But occasionally, by watching the gradual disappearance of one form after another, a hint may be gained with regard to the independence or association of any two groups of impulses.

Moreover, the tendency we have already noticed for the grosser forms of pain or discomfort to find a way to consciousness, although the more specific forms of pain, heat or cold are blocked, becomes more evident the closer the lesion lies to the optic thalamus. And yet it is probable that the impulses which evoke these uncomfortable sensations are not conducted by a bilateral path.

The following case, which we owe to the kindness of the late Dr. Beevor, illustrates the concentration of paths just before their entry into the optic thalamus. Incidentally it seems to show that the power of localizing the spot touched may be greatly affected at this level with but little loss of tactile sensibility.

CASE 4.—*Tumour of the mid-brain and optic thalamus verified by post-mortem examination.*

Five months before death the following signs were present—

Loss of power in the left arm and leg, with profound ataxy. Extensor response from left sole with normal response from right.

Athetoid movements of left hand, together with a fine tremor when the left arm was extended.

Eye-movements greatly restricted; nystagmus in all directions; fixed pupils.

The loss of sensation was confined to the left of the middle line. Sensations of prick were diminished over left arm and leg, but lost on the left palm only. Tactile sensibility was very little, if at all, affected during the time he was under observation by us.

Localization lost over left upper extremity. Compass-test gravely affected over left arm and leg. Appreciation of size and weight abolished in left hand.

T. B., aged 24, was admitted to the National Hospital on October 8, 1908, under the care of the late Dr. Beevor at the request of Dr. Judson Bury. After his death on July 24, 1909, his brain was described by Dr. Judson Bury [3].

In 1905 he began to see double and at the same time the lid of the right eye drooped. He recovered entirely, but in September, 1907, his eyelid drooped again and he became steadily worse. The left leg became weak about May, 1908, and in August involuntary movement began in the left arm. About the same time he noticed deafness in the left ear.

The following account of his condition was compiled from notes made by one of us between December, 1908, and the end of February, 1909.

Speech was not affected and he did not suffer from headache or vomiting. Neither pupil reacted to light or accommodation, and nystagmus was present with every movement of the eyes that could still be carried out. The right eye could be moved outwards but in no other direction; in the left eye movement inwards and outwards was still possible.

Vision in the right eye was $\frac{1}{16}$, in the left $\frac{8}{16}$; the fields were not diminished and both fundi were normal. Hearing was not materially affected either to aerial or bone conduction. Taste and smell were normal.

Movements of the face, jaws, tongue and palate were perfectly executed.

The arm-jerks were normal, but the right knee-jerk was brisker than the left; ankle-clonus could not be obtained on either side. The left plantar reflex gave an extensor response, whilst that from the right foot was definitely flexor.

All movements of the left arm and leg were less powerful than those of the right, but there was no paralysis and no increase of tone. Both left arm and left leg were profoundly ataxic and he could not stand on the left leg alone even with his eyes open.

If his eyes were closed or when his attention was distracted from the limb, the fingers of the left hand made characteristic athetoid movements, irregular slow extensions and flexions at the phalangeal and metacarpophalangeal joints. When the arm was extended, a fine tremor was also present in the left hand.

Condition of sensation.—The power of recognizing posture and passive movements of the left leg and arm was lost; he could not even find the left elbow with his normal hand. Told to open the fingers of his left hand when his eyes were closed, he made a series of irregular movements which partly extended the phalanges but flexed the metacarpophalangeal joints. The order to flex or to extend the fingers was followed by movements of this kind which led to no permanent alteration in posture.

Directly he was allowed to open his eyes, all movements of the fingers were carried out with ease, and so long as he looked at the hand, posture was maintained to command. Vibration was equally appreciated everywhere.

During the earlier period of our examination, he certainly appreciated the contacts of a test hair of 21 grm./mm.² all over the left upper extremity and on the left foot, showing that tactile sensibility could not have been gravely affected. But when cotton-wool or a measured hair were moved gradually from the right to the left half of the body, he said the stimulus became "lighter" to the abnormal side of the middle line.

Tactile localization was grossly affected over the whole left upper extremity, but on the lower extremity he indicated and named correctly the spot that had been stimulated. Thus, the disturbance of localization was here out of proportion to the diminution of tactile sensibility.

Spacial discrimination (compass-test) was gravely affected on the left upper and lower extremities; he was unable to recognize the two points when separated by 15 cm. on the left forearm and 20 cm. on the left half of the abdomen. On the normal arm 5 cm. and on the right half of abdomen 8 cm. gave perfect readings.

All power of recognizing size was lost in the left hand, and he could not even discriminate the head from the point of a pin.

He could not recognize the difference in weight between 5 and 200 grm. in the left palm.

Sensibility to prick was diminished over the left arm and the left leg, but

was nowhere absent except in the left palm. All the algometer readings were a little higher on the left than on the right half of the body, especially on the left palm and sole.

Sensibility to heat was absent on the left half of the body and face, but cold could be appreciated. The left leg, however, was insensitive to all degrees of heat and cold. Thus on the upper extremity temperatures above 45°C . evoked a sensation of paradox-cold, whilst on the leg they caused discomfort only.

Post-mortem five months after these notes were made.—The brain was examined by Dr. Judson Bury, who gave the following account of the condition [3]: "After being hardened in formalin the brain was cut into transverse vertical sections, when it was seen that the tumour occupied the position of the right optic thalamus and the corpora quadrigemina. The whole of the optic thalamus, with the exception of a thin layer on the outer side, was replaced by new growth which extended beneath the floor of the ventricle into the left optic thalamus for a short distance. The right internal capsule appeared to be normal, but no trace of the caudate nucleus could be discovered. The corpora quadrigemina appeared to be entirely replaced by growth; the crura and pons were also invaded. The right crus was considerably involved, so that a layer of the crusta only $\frac{1}{8}$ in. in thickness separated the growth from the basal surface of the brain. The anterior portion of the pons was invaded for about $\frac{1}{4}$ in. in depth on the right side and $\frac{1}{8}$ in. on the left side." The tumour was a large round-celled sarcoma.

Here, then, is a case where a malignant growth affected the corpora quadrigemina and that portion of the mid-brain at a point where the paths for sensory impulses are converging to end in the thalamus. The clinical signs indicate that this lesion started in the mid-brain, although at the time of death the right optic thalamus was also destroyed.

During the course of the disease this case showed that:—

In this situation the impulses underlying postural recognition, spacial discrimination and localization (spot-finding) may be dissociated from those concerned with touch and pain. At one stage of his illness the patient was therefore able to appreciate contact with von Frey's hairs and cotton-wool, but could not localize the spot touched. Nor could he tell the head from the point of a pin, or the relative size and weight of objects placed in his hand.

To sum up the conclusions of this section, we can say that the brain-stem between the nuclei of the posterior columns and the final termination of all sensory paths in the optic thalamus is the seat of the following changes:—

(1) The impulses for pain, heat and cold continue to run up in

separate secondary paths on the opposite side of the nervous system to that by which they entered. They receive accessions from the regrouped afferent impulses from the nerves of the head and upper part of the neck.

Although these paths are frequently affected together, they are independent of one another, and any one of the three qualities of sensation may be dissociated from the others by disease.

(2) Lesions of the spinal cord tend to diminish simultaneously all forms of painful sensibility, but with disease of the brain-stem the gross forms of pain and discomfort may pass to consciousness, although the skin is analgesic. This applies not only to painful pressure but to the discomfort produced by excessive heat.

(3) The impulses concerned with postural recognition part company with those for spacial discrimination at the posterior column nuclei. Up to this point, they have travelled together in the same column of the spinal cord, but as soon as they reach their first synaptic junction they separate. Above the point where they enter secondary paths, the power of recognizing posture and passive movement can be affected independently of the discrimination of two points and the appreciation of size, shape and form in three dimensions.

(4) It would seem as if those elements which underlie the power of localizing the spot touched or pricked become separated off from their associated tactile impulses before they have actually come to an end in the optic thalamus. The long connexion of localization with the integrity of tactile sensibility is here broken for the first time.

All these changes are preparatory to the great regrouping which takes place in the optic thalamus, and forms the subject of the following chapter.

CHAPTER II.—SENSORY DISTURBANCES ASSOCIATED WITH CERTAIN LESIONS OF THE OPTIC THALAMUS.

§ 1.—*Introduction.*

Throughout this work it has been our aim to discover the nature of the abnormal sensations evoked by disturbances at different levels of the nervous system. So far our task has been a comparatively easy one on account of the certainty with which the level of the lesion could be determined even in life.

We know that all afferent fibres passing upwards from the mid-brain end in the optic thalamus. Here lie the synaptic junctions of those

paths by which impulses are carried onwards to the cortex; no path passes upwards without undergoing a relay in some part of this organ. We shall now attempt to discover the changes in the grouping of afferent impulses which occur after they have terminated in the optic thalamus, and the part played by this organ in sensation.

It is obvious that, if all afferent impulses undergo a relay in the optic thalamus, a lesion at a point where they enter this organ may interrupt them before they have undergone regrouping: they may be cut off before they have reached the thalamic junction, and the loss of sensation would then correspond to that produced by a lesion of the mid-brain, although the disease might lie in the optic thalamus. On the other hand, sensory impulses may reach the optic thalamus undisturbed and undergo characteristic changes in grouping; but the fibres which conduct them from the thalamus to the cortex may be interrupted by the lesion. Finally, since lesions of the optic thalamus are usually of vascular origin and tend to disturb anatomical areas rather than functional paths, they not infrequently interfere both with the impulses which enter the thalamus and with those which pass away from this organ to the cortex.

Our business is to determine the nature of the sensory changes produced by interruption of sensory impulses at various points in their course, and for this purpose we must be able to recognize that a lesion is situated within the optic thalamus. This we can do, largely owing to the work of Dejerine and his pupils; for he pointed out first with Egger [6] and later with Roussy [7] that lesions, which involve the optic thalamus, are often characterized by a group of symptoms of which pain in the affected half of the body and other sensory disturbances form an integral part. These clinical symptoms and signs have been further elaborated by Roussy [35] and have been erected by him into a "syndrome thalamique." He has shown that a lesion of the optic thalamus may produce the following characteristic changes:—

(1) A persistent loss of superficial sensation of one half of the body and face. This loss to touch, pain and temperature is more or less definite, but the loss of "deep" sensibility is always more pronounced.

(2) Slight hemiataxy and a more or less complete astereognosis.

(3) Acute pains on the same side, persistent, paroxysmal, often intolerable, and yielding to no analgesic treatment.

(4) Slight hemiplegia which produces no contracture and rapidly passes away.

(5) Choreic and athetotic movements in the limbs of the affected side.

He pointed out that the sensory loss and the pains are alone due to the lesion of the optic thalamus, whilst the other symptoms are produced by destruction of surrounding parts.

Roussy has now established the anatomical significance of this "syndrome thalamique" by five *post-mortem* examinations. Others have been reported which show the truth of Dejerine's original generalization (Long [21], Winkler and van Londen [42]).

The following case exactly fits into Roussy's category:—

CASE 5.—Mrs. C. H., a woman, aged 51, was suddenly seized with pain on May 28, 1908, which spread from the upper part of the chest over the left arm. Twenty minutes later the arm became numb. She then lost consciousness for a few minutes, and, when she came to herself, found she could not move the left arm and leg.

The hemiplegia rapidly passed away, and is now represented solely by the exaggerated reflexes on the left half of the body. There is a tendency to ankle-clonus in the left foot, and the plantar reflex is of the extensor type. Both the left arm and the left leg are gravely ataxic, and curious spontaneous movements are of constant occurrence in the left arm. They are particularly liable to be started or aggravated by any stimulus which evokes the unpleasant sensation and then continue apart from further excitation.

Ever since this "stroke," she has suffered from pains in the left half of the body, and an uncomfortable sensation as if something were crawling under her skin. These pains are intense in the hip, the loin and under the left shoulder. They are said "to pump up and down the side" and the left arm and leg "feel as if they were bursting." Whenever there was cause for visceral discomfort, such as the passage of a constipated motion, these pains became particularly severe, and the heart is said to "throb" and the stomach to "work" painfully, but on the left side only.

Sensibility to light touch and to temperature is diminished but not completely lost over the left half of the body. She is totally unable to distinguish the two points of the compasses when separated to many times the normal distance, and localization of both tactile and painful stimuli is gravely defective. Discrimination of shape, weight, and consistence is impossible, and she cannot appreciate the nature or use of objects placed in her left hand. The power of recognizing relative size is affected, but it is possible to obtain a difference-threshold even on the affected side (*vide* p. 143.)

Painful or disagreeable stimuli, such as the prick of a pin, painful pressure and the extremes of heat and cold, all produce more discomfort on the left (affected) than on the right half of the body, and are liable to increase the permanent pains and tingling, of which she so greatly complains. And yet the strength of the prick necessary to produce pain, measured with the algometer, is the same on the two sides and the readings of the pressure-algometer differ little over normal and affected parts.

The recognition of posture and of passive movement is gravely affected in the left arm and left leg, and active movements of both limbs are ataxic.

Here, then, we have an instance which exactly corresponds to Roussy's description of the "syndrome thalamique," for not only were certain qualities of sensation definitely diminished but spontaneous and intractable pains were present on the affected half of the body.

In the following case, where the site of the lesion was verified by autopsy (No. 6), the loss of sensation was extreme, but the patient suffered from the same intense pains.

CASE 6.—A man, aged 49, was suddenly seized with right hemiplegia six months before he came under observation. When he was first seen there was little paresis, and the reflexes, though brisk, were not abnormal. Speech was unaffected. He complained, however, of severe aching cramp over the whole right half of the body, of pain and soreness in the right arm and a crushed feeling in the right foot.

Sensibility both to light touch and to pressure was abolished, and he could not recognize posture or passive movement on the right half of the body; all appreciation of weight was lost in the right upper extremity. He failed to recognize all degrees of temperature, but ice and water at 60° C. produced intense discomfort, much greater on the affected than on the normal side.

A stronger prick and greater pressure of the algometer were required to cause pain on the affected parts, but, when once evoked, the pain was much less bearable and produced a stronger reaction.

The only lesion, discovered at the autopsy, to which these symptoms could have been due was a softening of the lateral zone of the optic thalamus.¹

We have observed twenty-four more or less similar cases, with sufficient symptoms and signs to justify us in diagnosing a lesion in the optic thalamus such as Roussy has described. In some the loss of sensation was less than that in Case 5 and in others it was even more profound than in Case 6.

The loss of sensation differs in no way from that produced by interference with sensory impulses, either as they enter the optic thalamus or as they pass to the cortex by way of the internal capsule. But to these familiar defects another factor may be added when the lesion destroys certain parts of the optic thalamus. This fresh factor, which alone can be attributed to the disturbed activity of this organ, is a tendency to react excessively to unpleasant stimuli. The prick of a pin, painful pressure, excessive heat or cold, all produce more distress than on the normal half of the body, and this is the essential feature in all the cases with which we shall deal in this chapter. There are other cases, where the optic thalamus is destroyed, in which the spontaneous pains

¹ For a fuller account of this case see p. 255 of this number of BRAIN.

and the characteristic over-response are absent; but with these we are not concerned at present.

§ 2.—*The Excessive Response to Affective Stimuli, and the Behaviour in States of Emotion, of the Abnormal Half of the Body.*

(A) *The Response to Unpleasant Stimuli.*

(a) *Prick.*

We have cited Mrs. H. (Case 5) as a characteristic instance of the "syndrome thalamique" described by Roussy, and we shall now proceed to investigate her behaviour to measured painful stimuli.

If a pin is lightly dragged across the face or trunk from the right to the left half she exhibits intense discomfort when it passes the middle line; she not only calls out that it hurts her more, but her face becomes contorted with pain. But she insists that, although the stimulus is more painful, it is "less plain" and "less sharp" than over normal parts; the prick is less distinct but it hurts her more.

This "hyperalgesia," or over-reaction, would seem to point to a lowered threshold to the prick of a pin. But measured stimulation with both the spring and the weight algometers shows that, if anything, the threshold is a little raised; she never responds with certainty over the abnormal (left) half of the body to a stimulus which can evoke a sensation of pricking on similar normal parts to the right of the middle line. And yet, if a measured stimulus of the same strength is applied to similar parts, more pain is evoked over the affected than over the normal half of the body; the same stimulus, provided it is sufficiently strong to cause pain, produces a more uncomfortable sensation on the abnormal side.

This remarkable over-response to prick was present in twenty out of twenty-two patients in whom the strength of the stimulus was carefully measured. But in no instance was the threshold lower on the affected half of the body; in thirteen cases it was identical on the two sides, and in nine a decidedly stronger stimulus was necessary to produce a sensation of prick, in spite of the greater discomfort experienced by the patient when pain had once been evoked.

(b) *Painful Pressure.*

Throughout our work we have attempted in every case to measure the amount of pressure which evoked pain. Cattell's algometer was

applied to similar parts on the two halves of the body, and the point was registered at which the pressure became uncomfortable.

Now in the class of case with which we are concerned in this chapter, pressure is peculiarly liable to produce greater distress and an increased reaction on the affected side. Out of twenty-four patients every one responded more violently to painful pressure, and all complained that the same pressure, if it evoked discomfort, was more disagreeable on the abnormal than on the normal half of the body.

Moreover, this pain did not develop gradually out of the painless sensation of pressure as on the normal side, but seemed, over the affected parts, to develop explosively. Up to a certain point the patient remained unconcerned, but suddenly, as the pressure increased, he would cry out and withdraw the limb to which the instrument was applied; from the expression of his face, he had obviously been more hurt than by the same pressure on the equivalent normal part.

This increased reaction is frequently, though not necessarily, associated with a lowering of the threshold; the same pressure may be required on both sides to evoke pain, although the response on the affected half of the body is excessive (six cases). In three cases, including the one which came to *post-mortem* examination, the threshold was actually higher on the side of the greater reaction; the following readings were obtained, amongst others, from the palm and sole, in this case:—

			Right (affected)				Left (normal)		
Palm of hand	..	..	15	12	11	..	8	8	8
Sole of foot	..	..	9	9	10	..	5	4	4½

Thus, although more pressure was required to elicit pain from the right than from the left half of the body, the discomfort produced was manifestly greater on the abnormal side.

Although this increased reaction may occur with a normal and even with a raised threshold, we found that in fifteen out of our twenty-four cases the pressure necessary to cause discomfort was less on the affected side. This was particularly the case on the palm and sole of the foot. But in spite of this lowering of the threshold to painful pressure, not one of these cases showed a lower threshold when the stimulus was a prick. Obviously, the pain produced by excessive pressure contains some sensory factor to which the abnormal half of the body is peculiarly susceptible.

Now, if anyone will apply the algometer to his own hand or foot, he will find that the pressure causes discomfort rather than pain. There is something terrifying about the crushing sensation, especially when a

bone is pressed upon. The condition evoked is less a pain than an unbearable and distressing sensation, and in this way differs profoundly from the prick of a sharp point. Both stimuli produce pain and discomfort; but, whereas a prick produces a sensation of pain associated with more or less discomfort, pressure upon bones and other deep structures evokes more discomfort than formal pain.

In these cases of over-reaction on the affected half of the body, it is susceptibility to the uncomfortable element of a stimulus which is increased, rather than sensibility to pain. Not uncommonly, the threshold may be actually raised to prick but lowered to pressure-pain, although both stimuli produce greatly increased discomfort over abnormal parts.

Any loss of sensibility to pain delays the appearance of this over-reaction; but as soon as the stimulus is strong enough to cause pain, the discomfort will greatly exceed that produced by the same stimulus over normal parts.

(c) *Extremes of Heat and Cold.*

Wherever this over-reaction to painful stimuli exists, the response to the more extreme degrees of heat and cold is usually changed. Thermal appreciation may be unaltered, may be diminished, or may be actually lost, and yet the discomfort produced by cold and hot water will be greater on the affected than on the normal half of the body.

In the case we have cited above (Case 5), thermal sensibility was diminished, but the response was more intense on the affected side. All temperatures between about 27° C. and 46° C. were less cold or less hot over the affected parts. But everything above about 47° C. and below about 26° C. was thought to be hotter or colder than on the normal side. The more the temperature of the stimulus sank below or rose above these limits, the more uncomfortable it became on the affected half of the body, compared with normal parts. We shall show later that there is in all probability no actual increase in sensibility to heat and cold at these temperatures; the patient translated the increased discomfort into terms of greater cold and heat.

All sensibility to heat and cold may be lost, and yet this over-reaction may still occur on the affected side. But in such cases the stimulus must be intense; the heat applied must be above 50° C., and the cold required will usually lie below 15° C., and sometimes even melting ice is necessary to evoke this over-reaction. But when once a stimulus has

been found capable of producing a response, the discomfort is excessive on the affected half of the body.

In these extreme cases the discomfort may not be expressed in terms of heat and cold. For instance, in Case 6, ice and temperatures above 55° C. produced an intense reaction. The patient's face was contorted as if in pain, and he cried out, "Oh, something has caught me"; "something is forcing its way through me, it has got hold of me, it is pinching me."

To the most interesting group, however, belong those cases where an excessive response was evoked on the affected side, in spite of a thermal sensibility otherwise perfect. In Case 8 (p. 219), for instance, the threshold for the appreciation of heat and cold was identical on the two halves of the body, but whenever a stimulus produced any but the mildest sensation of cold, it seemed "colder" and more unpleasant over the affected than over the normal palm. A stimulus recognized as warm did not become "hotter" on the affected hand, until it was raised to between 40° and 45° C.

Thus, in conclusion, whenever a thermal stimulus can produce discomfort, this will be greater on the affected than on the normal side. Should the appreciation of heat and cold be sufficiently preserved, this discomfort will be thought to imply a higher or a lower grade of temperature in the stimulating object; it will seem "hotter" or "colder" than the same temperature on the normal side. If thermal sensibility is equally perfect on the two halves of the body, the excessive response will begin as soon as the stimulus seems definitely cold. But it will not seem "hotter" on the affected side, until the temperature of the stimulus reaches about 45° C. or above.

(d) *Visceral Stimulation.*

Discomfort in its purest form is produced by stimulation of the viscera, and we therefore compared the condition of testicular sensibility on the two sides in patients who showed this over-response to painful stimuli.

If care is taken not to pinch the scrotum, the characteristic testicular sensation, a sickening discomfort, can be evoked with no other accompaniment than a sensation of not unpleasant pressure. Many patients complained that the discomfort was more intense in the testicle of the affected side. Pressure, sufficient to produce "a slight feeling" only on the normal side, caused a widespread expression of discomfort and brisk cremasteric movements of the testicle on the affected half of the body.

The glans penis is endowed with a peculiar form of sensibility which differs normally from that of the skin in the absence of the more discriminative faculties (Rivers and Head [33]). Heat and cold can be distinguished, but the finer grades of temperature are not appreciated. A prick causes a more widely spread sensation and is more unpleasant than over the rest of the normal skin. In fact, the glans penis is an organ endowed chiefly with the more affective elements of cutaneous sensibility, and it is therefore a peculiarly appropriate field for examination in cases which exhibit the over-reaction on the abnormal side.

When the glans is pricked with such an instrument as the algometer, the same strength of stimulus may be necessary to evoke pain on the two halves of the organ; but the discomfort described by the patient and obvious from his expression is greater on the abnormal than on the normal portion.

(e) *Scraping, Roughness, Vibration.*

All the stimuli, considered so far, contain for the normal person some obvious element of pain or discomfort. But, in these cases of over-reaction on the affected side, scraping the palm or the sole of the foot, moving a rough object over the skin, or even rubbing the hairs, may evoke an unpleasant sensation, unlike that from the normal half of the body.

The difference between the two sides is, as a rule, most evident when the observer gently scrapes with his fingers the patient's palm. Under normal conditions this is not unpleasant; but on the affected side the patient may cry out and attempt to withdraw his hand. His face is contorted with discomfort. One patient complained: "It is a horrid sensation, as if my hand were covered with spikes and you were running them in; it is not painful but very unpleasant." Frequently this sensation spreads widely, running up the arm or the leg, and is often started with peculiar ease from the sole of the foot (Roussy [36], Case 1).

This excessive response to scraping is frequently a striking feature during examination with the Graham-Brown æsthesiometer. This instrument serves to estimate the appreciation of roughness by measuring the extent to which a tooth must be protruded from a spherical surface in order that it may seem "not smooth." We not uncommonly found that the "raking" sensation produced by this instrument was greatly exaggerated on the affected half of the body. But in no case was the threshold lowered. In some it was equal on the two sides,

and in others a greater protrusion was required to evoke a sensation; but in the large majority the discomfort produced was greater on the affected side. Occasionally, even the rubbing of the smooth surface over the affected parts caused an uncomfortable tingling, which confused the patient and rendered measurement impossible. In one case the instrument produced no sensation of roughness, but the tingling and discomfort were intense.

Many of these patients complained that they could not be shaved on the affected cheek because it seemed as if the razor was "passing over a raw surface." Some objected to having the hair cut on the affected half of the head, because of the discomfort, and others complained of the pain caused by the attempt to cut their nails.

Occasionally even the vibration of the tuning-fork may give rise to an unpleasant sensation, which spreads widely over the affected half of the body (Roussy [35], Case 1).

Thus, in cases where the affected parts react more strongly to painful stimuli, it may happen that even scraping with the fingers, the application of rough objects to the skin, shaving, cutting the hair or nails, or even the vibration of a tuning-fork may cause discomfort or produce a more unpleasant sensation than on the normal side.

(f) *Tickling.*

When the tips of the fingers are gently moved over the palm or the sole, or when the ears and other hair-clad parts are stimulated with cotton-wool, a tickling sensation can be produced in most normal persons. This is not unpleasant, and in some people the movements of withdrawal which result are accompanied by smiles of amusement. But in those cases characterized by an over-response to painful stimuli tickling is usually unpleasant. Several patients insisted that the sensation produced on the normal side was not disagreeable, whilst that from the abnormal parts was quite different and unpleasant. In all such cases the reaction was greater on the affected half of the body.

(B) *The Response to Pleasurable Stimuli.*

So far we have considered over-reaction of the affected half of the body to stimuli which are in themselves unpleasant, or are capable under certain conditions of evoking an unpleasant sensation. We were anxious to discover if sensations, normally accompanied by a pleasurable feeling-tone, also produced a similar over-reaction.

Unfortunately, the greater number of the methods applicable for the measurement of sensibility either produce discomfort or, like the tests for weight and for posture, evoke an entirely indifferent sensation. But in the milder degrees of heat we possess a measurable stimulus endowed with a pleasant feeling-tone. In the majority of cases, however, which showed an over-reaction to the uncomfortable aspect of a stimulus, sensation was at the same time more or less gravely lost; and this loss was particularly liable to fall upon that portion of the thermal scale, which normally yields a sensation of pleasant warmth; in such cases this test is usually inapplicable.

On the other hand, in a few cases when thermal sensibility was abolished, warmth applied over a sufficiently large surface evoked a feeling of pleasure. Thus, one of our patients found a hot-water bottle pleasant and soothing to the affected foot, but did not recognize that it was warm until he touched it with some normal part. In the same way, many patients found the warm hand of the observer unusually pleasant on the abnormal side, although no such manifestations of pleasure were produced when it was applied to normal parts of the body. In one case, we were able to show that the patient could not recognize any thermal stimulus as such, and yet over the affected half of the chest large tubes containing water at from 38° C. to 48° C. evoked intense pleasure. This was shown not only by the expression of her face but by her exclamations, "Oh! that's lovely, it's so soothing, so very pleasant." Temperatures of 50° C. and above, or of 18° C. and below, caused great discomfort exactly as in most of these thalamic cases (*vide* p. 226).

Several of our patients, however, were able to appreciate heat as low as 34° C. on the affected half of the body. Here, whenever the sensation evoked was one of pleasant warmth, the pleasure was obviously greater on the affected side. In one case, a tube containing water at 38° C. applied to the normal palm was said to be warm; but the patient cried out with pleasure when it was placed in the affected hand. His face broke into smiles and he said, "Oh! that's exquisite," or "That's real pleasant." Another patient said, "It seems warm on both hands, but it is more soothing, more pleasant on the affected palm."

The following observations were made on an intelligent and highly educated man. We determined the threshold for the appreciation of heat on the two hands. It was found to be the same, although both the pleasure given by the lower degrees of heat and the discomfort produced by the higher degrees were exaggerated on the affected palm. We

then attempted to discover at what point unpleasant heat became converted into pleasant warmth. On the affected hand a temperature of 50° C. was "too hot," "very unpleasant," whilst it was "not so hot" on the normal palm; 48° C. was still "too hot," but 45° C. became "real pleasant," although it was "simply warm" on the other side. Thus in this case excessive pleasure was converted into excessive discomfort at about 46° C. This is the temperature at which, on introspection, we are conscious that hot water gains a "sting" absent from the lower degrees.

Cold has no pleasurable element, at any rate during the greater part of the year in this country. As soon as a sensation of cold is produced it is said to be "colder" and "more uncomfortable" on the affected half of the body. The threshold, or point at which a stimulus is said to become cold, generally lies somewhere between 24° C. and 27° C., and, as soon as the sensation of coldness is well developed, this discomfort begins. So far we have been unable to find any temperature which produces a sensation of pleasurable cold.

Thus, in conclusion, we find that in cases where the pleasurable aspect of heat can be appreciated, the pleasure is accentuated on the affected side; yet the threshold for the appreciation of heat is never lowered and may even be raised on the side of the excessive reaction.

(C) *The Behaviour of the Affected Half of the Body in States of Emotion.*

In the preceding sections we have seen that the two halves of the body respond differently to affective stimuli. But no one seems to have recognized that states of emotion may evoke different manifestations on the two sides; not only can pleasant and painful stimuli produce a stronger reaction when applied to the affected parts, but the two halves of the body may behave differently to mental states of pleasure and discomfort.

Music is peculiarly liable to evoke a different reaction on the two halves of the body. One of our patients was unable to go to his place of worship, because he "could not stand the hymns on his affected side," and his son noticed that during the singing his father constantly rubbed the affected hand.

Another patient (Case 11, p. 227) went to a memorial service on the death of King Edward VII. As soon as the choir began to sing, a "horrid feeling came on in the affected side, and the leg was screwed

up and started to shake." The characteristic, so-called choreiform, movements were a prominent feature in this case, and whenever the unpleasant sensation was evoked in the affected side these movements were accentuated. The singing of a so-called comic song left her entirely cold, but "A che la morte" produced so violent an effect upon the abnormal half of the body that she was obliged to leave the room. In this case indifferent sounds, such as the note of a tuning-fork or sound of a bell, produced no abnormal effect, and closing the ear of the affected side made no difference to the character or intensity of the response.¹

A highly educated patient confessed that he had become more amorous since the attack, which had rendered the right half of his body more responsive to pleasant and unpleasant stimuli. "I crave to place my right hand on the soft skin of a woman. It's my right hand that wants the consolation. I seem to crave for sympathy on my right side." Finally he added, "My right hand seems to be more artistic."

Thus, not only does the abnormal half of the body respond more vigorously to the affective element of a stimulus, but an over-reaction can also be evoked by purely mental states. The manifestations of this increased susceptibility to states of pleasure and pain are strictly unilateral and may lead to many curious complications.

§ 3.—*The Loss of Sensation which may be associated with Lesions of the Optic Thalamus.*

Associated with this over-reaction to painful stimuli, some loss of sensation will always be manifest on the affected half of the body. In some cases, the amount of this loss is so insignificant that, as it can be discovered by measurement only, we can imagine the existence of the over-reaction without it. But up to the present time we have not seen a patient in whom this excessive response was not accompanied by some sensory loss. It may vary in amount from a diminution so slight that it is scarcely recognizable, up to a destruction of all

¹ Occasionally, however, auditory stimuli produce an increased reaction on the affected side exactly in the same way as pain and extremes of temperature. Such a case was described by Merle [24], and we have seen an instance of this condition (Case 12, p. 230). This patient complained that any continuous sound and all noises upset him. When a tuning-fork was held before either ear it evoked obvious discomfort and gradually became intolerable. At the same time the spontaneous movements became extremely violent. It was difficult to be sure that the fork placed before one ear was a more potent cause of discomfort and exaggerated movement in the affected arm than when it was placed before the ear of the opposite side; but after testing him on many occasions, we came to the conclusion that the effect was greater if the sound affected the ear on the abnormal side of the body. There was, however, no doubt that he disliked the sound more in this ear than in the normal one.

forms of sensibility so severe that only the grossest stimuli can be perceived.

The vehemence of the excessive response bears no relation to the extent of the accompanying loss of sensation. Sometimes, severe discomfort may be evoked by affective stimuli in cases where sensibility is grossly diminished; but many patients with but slight loss suffer great discomfort, for the existence of a sensibility of approximately normal acuteness opens the way to the reception of more impulses that can evoke an excessive response.

(a) *The Appreciation of Posture and Passive Movement.*

With lesions of the optic thalamus and neighbouring parts, the appreciation of posture and passive movement suffers more frequently than any other sensory quality. Sometimes, the ordinary rough tests reveal no obvious defect, although measurement shows that the recognition of the position of the hand, or the power of appreciating passive movement, is less accurate on the affected side. Thus in one case passive movements of the normal index were appreciated within a range of from 3° to 3.5° (flexion, average 3.5° ; extension, average 3°), whilst on the affected side, movement was not recognized under from 7° to 8° (flexion, average 8° ; extension, average 7°). At the opposite pole stand such cases as No. 6, a patient in whom the lesion was determined *post-mortem*. This man was totally ignorant of the position of his right arm and leg, and could not recognize passive movement as such in the limbs of the affected side.

Between these two extremes all grades of diminished appreciation of posture and of passive movement could be discovered. These two functions were always found to be affected together, except in two cases, where the defect in the appreciation of passive movement was slight and lay close to the limits of experimental error.

(b) *Tactile Sensibility.*

Here again we find the same extraordinary divergence in the amount of the sensory loss. In five cases the tactile threshold, measured with von Frey's hairs, was identical on the two hands; but, in the majority, some more or less grave deviation from the normal was discovered on the affected side. Sometimes, the affected parts are entirely insensitive to the tactile hairs and even considerable pressure may not be appreciated.

But frequently the loss of tactile sensibility is much less extreme and is manifested simply by a raised threshold. Sometimes, the normal

hand responded with certainty to a hair of 21 grm./mm.², whereas from 70 to 100 grm./mm.² was required on a similar part of the affected side to evoke a perfect series of answers. The following records illustrate this condition.

	Left (normal)	Right (affected)
21 grm./mm. ²		
21 grm./mm. ²		000 000 000 000
23 grm./mm. ²		0 0 0 0 0 0 0 0
35 grm./mm. ²		1111 0 0 0 0
70 grm./mm. ²		1111111111
23 grm./mm. ²		1 0 1 0 1 0 1 0
21 grm./mm. ²		000 0 0 000 000
21 grm./mm. ²		

				Left (normal)		Right (affected)
21 grm./mm. ²	..	..	..	16 out of 16	..	—
21	..	..	..	—	..	4 out of 16
28	..	..	..	—	..	8 „ 16
35	..	..	..	—	..	13 „ 16
70	..	..	..	—	..	16 „ 16
23	..	..	..	—	..	12 „ 16
21	..	..	..	—	..	5 „ 16
21	..	..	..	16 out of 16	..	—

Occasionally, the consecutive contacts necessary for this test caused the widespread tingling to which these patients are prone. This may make it impossible to demonstrate the threshold conclusively. Increasing the strength of the stimulus will increase the number of correct answers, but the persistent tingling confuses the patient and he frequently replies when he has not been touched.

Another difficulty that may prevent the demonstration of a tactile threshold, by means of von Frey's hairs or with graduated pressure, is the occurrence of involuntary movements. Many of these patients show curious irregular movements which may not always be present, but are liable to start again when the affected side is stimulated. Movements arising involuntarily may be mistaken under these conditions for touches. The longer the testing is continued the more accentuated these movements become, and demonstration of a threshold is then impossible.

To sum up, the tactile threshold may be normal on both sides in the cases with which we are dealing in this chapter; or it may be raised to a greater or less extent, even up to complete abolition of

sensibility to measured tactile stimuli. Accessory sensations or the misinterpretation of involuntary movements may confuse the records, but the loss of threshold and the irregular response, so characteristic a consequence of cortical lesions, is not found as the result of destruction at this level of the nervous system.

(c) *Localization.*

The power of recognizing the position of a stimulated spot was more or less grossly affected in twelve out of twenty-four cases. This faculty may be so profoundly disturbed that a touch on the hand is referred to the same half of the face or trunk. More commonly, the patient complains that he has no idea where he has been touched. "I feel you touch me, but I can't tell where it is; the touch oozes all through my hand." Although the method¹ we have generally used forces him to recognize that he has been touched somewhere on the hand, the patient frequently gives up all attempts to determine the spot, saying, "I have no idea where you touched me."

In cases of graver loss of sensation, tactile sensibility is not infrequently much diminished, but the inability to localize the stimulated spot is equally great, even with a prick or with painful pressure, to which the patient is acutely sensitive.

When all power of localization is abolished and the posture of the limb cannot be recognized, sensations may be no longer referred to something outside the body; they are thought to be due to some change within the part rather than to an external stimulus. When the hand was scraped one of our patients said, "It is as if something inside the arm were moved, not like anything touching me." Sometimes the sensation was said to be "a cramp inside my arm."

Wherever localization is affected, the unpleasant sensation evoked by painful stimuli may spread widely over affected parts. When, for instance, the sole has been pressed with the algometer, the pain may occupy the whole of the leg below the knee, and the patient does not recognize that the instrument was applied to his foot. No matter what stimulus may have evoked the unpleasant sensation, it will spread widely if the faculty of localization is destroyed. The power of recognizing the position of the stimulated spot seems to exert an inhibitory influence on the distribution of this uncomfortable sensation. Appreciation of the locality of the site from which the sensation has been evoked tends to confine it to the neighbourhood of that spot, and around this it radiates to a limited extent.

¹ See discussion on this method on p. 198.

(d) Heat and Cold.

Twenty-two out of twenty-four patients who showed signs of a thalamic lesion responded excessively to the unpleasant aspect of heat and cold. In nine of these cases the threshold for thermal stimuli was the same on the two sides, and but for the over-response sensibility to heat and cold appeared to be normal; the range of discrimination was identical on the two halves of the body. This class is peculiarly interesting, for in them may appear the remarkable over-response to pleasurable heat we have described on p. 134.

But, not infrequently, all appreciation of heat and cold is abolished and ice and water at over 50° C. evoke nothing but discomfort. This sensation is the same, whichever of the two extremes is used; the patient cannot tell the difference and may not recognize the cause of the unpleasant sensation.

Occasionally, the insensibility is less profound and temperatures below 26° C. and above about 40° C. may evoke a response from the affected half of the body. But this response may be the same for heat and cold; water above 40° C. and below 26° C. produces the same sensation and may therefore be called indiscriminately hot or cold. For, if the patient knows from the experience on his normal side that thermal sensibility is under examination, he concludes that this vivid sensation is caused by "something hot" or "something cold." No such confusion between the extreme degrees of heat and cold ever occurs when the patient is able to distinguish intermediate degrees.

We have seen no reason so far to think that at this level of the nervous system the power of appreciating either heat or cold can be lost alone. The few apparent exceptions were due to the adoption by the patient of the same thermal nomenclature for the unpleasant reaction produced by certain temperatures towards the two ends of the scale, a confusion rendered possible by the absence of thermal appreciation.

Sometimes the disturbance of sensibility to heat and cold is less severe; temperatures above 38° to 40° C. are recognized as warm and those below about 26° to 28° C. as cold. Under such conditions any temperature that can be appreciated is thought to be respectively "hotter" or "colder" on the affected side, and yet there is no evidence that the supposed greater heat or cold is due to anything but the increased affective reaction.

Throughout all these cases, where the loss of thermal sensibility was not absolute, a threshold could always be determined. It might be the

same on the two sides, or it might be more or less raised on that half of the body which showed an excessive response. But never did we find that remarkable loss of threshold and inability to discriminate between two temperatures, both of which were recognized to be hot or to be cold, so characteristic a feature with cortical lesions.

(e) *The Compass-test.*

In order that this test may be applied, the patient must of necessity be able to recognize that he is being touched; tactile sensibility must not be gravely diminished. But many of the patients, who reacted excessively to painful stimuli on the abnormal side, were so insensitive to touch and pressure that the contact of two points produced no sensation and the compass-test could not be employed.

Another disturbing element in these cases is the widespread unpleasant tingling frequently evoked by a firm touch; this tingling is liable to distract the patient's attention and confuse the records greatly.

Excluding these sources of error, a considerable number of cases still remain in which the power of recognizing the "two-ness" of the compass-points was disturbed although each touch evoked a sensation of contact. But, by widening the compasses, a distance could usually be found at which a perfect series of answers could be obtained, and the records improved each time the distance of the two points from one another was increased. Thus in such cases it is possible to obtain a true threshold.

In most of these cases, it is true, tactile sensibility, as measured by von Frey's hairs, showed a somewhat raised threshold. But the discrimination of the compass-points is not directly dependent on tactile sensibility, although at this level of the nervous system they may rise and fall together. For, if two sharp points are substituted for the blunt ends of the compasses, the difficulty in recognizing them is just as great, although each prick produces a more profound effect over the abnormal half of the body.

Thus, in conclusion, we have found that the compass-test could not be applied in many of these cases, owing to the gross loss of tactile sensibility or to the confusion produced by the abnormal tingling. But whenever the measured tactile threshold was the same on the two halves of the body the power of discriminating two points was unaffected; and yet the two faculties are not directly dependent, for two pricks cannot be discriminated more easily than the contact of two blunt points.

(f) The Appreciation of Weight.

Throughout this research we have adopted three methods of testing the appreciation of weight. A weight is placed in each palm and the patient by moving them up and down "weighs" them and estimates which is the heavier. Secondly, a weight is placed on some part of the fully supported hand, removed, replaced rapidly by another weight of the same size, and the patient chooses the heavier. Lastly, a weight is placed upon the hand and further weights are added or subtracted. The patient replies whenever he recognizes that the weight has become heavier or lighter.

Now it is obvious that the last two methods depend mainly upon an appreciation of relative pressure, whereas the first demands a power of estimating movement and the force employed in lifting the weight.

At the level of the nervous system with which we are now engaged this difference comes out in a remarkable manner. In some cases the only discoverable loss of sensation consisted in a diminished recognition of posture and passive movement, and correlated with this loss was an inability to distinguish weights placed simultaneously on the unsupported hands; and yet the patient may be able to recognize the relation between two weights, placed one after the other on the affected hand when fully supported.

Conversely, any diminution of tactile sensibility at once affects the power of appreciating relative pressures, and so interferes first with the estimation of weights applied consecutively, and later even with the ability to recognize whether an object resting on the palm has become heavier or lighter. In one case the tactile threshold was slightly raised, but all forms of postural recognition were perfect; here estimation of consecutive weights and recognition of the increase or diminution of a weight resting on the supported hand were both somewhat affected. But appreciation of the relative heaviness of two weights placed one in each unsupported palm was not disturbed.

Thus, at this level of the nervous system the power of estimating the relation between two weights depends on the integrity of both tactile and postural impulses. The faculty of estimating the relative weight of two objects placed one in each unsupported hand demands a correct appreciation of posture and movement. But appreciation of two weights placed consecutively on the supported hand, and the power of recognizing addition to, or removal from, the weight of an object lying in the palm, require a normal tactile sensibility.

(g) *The Appreciation of Size, Shape and Form in Three Dimensions.*

No tests for the recognition of size, shape, or form can be applied unless the patient is able to appreciate the contact of objects placed in his palm. In five of our cases this was impossible, owing to gross loss of tactile sensibility, whereas, on the contrary, in six cases the lesions which produced an over-response to painful stimuli had in no way affected the power of recognizing size, shape or form.

Between these two extremes lies a group in which all three forms of recognition were more or less gravely defective. Although the defective recognition of size, shape and form in three dimensions, which may accompany the over-response to painful stimuli, appears at first sight to resemble that due to cortical lesions, more careful examination shows that they may differ fundamentally from one another. Ordinary clinical tests, employed in the usual rough manner, are incapable of demonstrating this difference. But, when a series of tests are carefully carried out, the patient is able, in most cases, to recognize a difference in size, provided it is sufficiently large; a true difference-threshold can be obtained. He does not give up all attempts to estimate the relative size of the test-objects, saying, as in the case of a cortical lesion, "I have no idea." He may make mistakes in their relative size or may believe that the two objects are equal, but retains an impression that they possess a size to be compared. Ultimately, if the difference between them is made sufficiently great, his answers grow increasingly more accurate.

For instance, in the following set of observations (Case 5), it will be seen that the patient could appreciate a difference in two circular test-objects, when the diameter differed by 2 cm., but not when the one exceeded the other by 1 cm. only. She could recognize a difference of 1.5 cm. when the diameters were 3.5 cm. and 2 cm., but not when they were 4 cm. and 2.5 cm.

				Normal palm		Affected palm:	
2	cm.	and	3	..	..	Four right	.. Four wrong.
3	"	"	4	"	"	"	.. Two right, two wrong.
4	"	"	2.5	"	"	"	.. One right, three wrong.
4	"	"	2	"	"	"	.. Four right.
3.5	"	"	2	"	"	"	.. "
5	"	"	2	"	"	"	.. "

Here it is obvious that increasing the difference improved the accuracy of the answers, and a true difference-threshold could be worked out approximately, even with so small a number as twenty observations.

Unfortunately, we have no method of reducing the tests for shape and form in three dimensions to measure in the same way. For increasing the size of objects used for testing shape beyond certain limits prevents their uniform application to the palm, and any considerable

reduction makes it impossible to recognize them on the normal hand. Even the size of the objects used as tests for form in three dimensions cannot be varied greatly, since it is necessary that the patient should be able to roll them between his fingers and palm.

In spite of these difficulties the patient usually attempted to give some name to the object, provided tactile sensibility was not greatly impaired, and he could move it to and fro in his hand. Not uncommonly he said, "I have an idea of the shape, but it seems numb." Moreover, in the majority of instances a certain number of right answers were given, especially to the easier tests, such as the circle or the sphere, and the familiar objects commonly used in clinical examination were frequently recognized.

Thus, in conclusion, we find that in these cases the recognition of size, shape and form in three dimensions may be intact, or more or less gravely affected. In some instances, this loss of recognition is due to gross defects in tactile sensibility. But in a considerable group of cases the difference-threshold is raised; here all idea of size, shape, and form is not abolished, as in the cortical cases, but a greater difference than normal is necessary before they can be appreciated. In the same way, the patient retains an idea that the objects have a shape and form, but finds difficulty in recognizing what it may be.

(h) Vibration.

The loss of sensation must be unusually gross before the vibrations of a tuning-fork cease to be appreciated. In three cases only was the affected half of the body insensitive to this stimulus, and in all of them most other forms of sensation were gravely affected.

Usually the vibrations of the tuning-fork are appreciated on both halves of the body, but the stimulus appears to last a shorter time on the abnormal side. If the tuning-fork is placed upon some point of the affected side and, as soon as it can no longer be appreciated, is rapidly transferred to a corresponding part on the normal half of the body, the patient will continue to recognize the vibration for a further period, which may even extend to fifteen seconds. This shortened appreciation of the tuning-fork is one of the most characteristic features of the loss of sensation associated with the over-response to painful stimuli. It occurred in fifteen of our cases, and was independent of that unpleasant feeling-tone evoked by vibration, of which we have already spoken.

At the same time the patient complains that the vibrations are "not so plain" on the abnormal half of the body and in certain cases the fork seems to be vibrating less rapidly on the affected side.

(i) Roughness.

In three cases only was the loss of sensation sufficiently gross to prevent the appreciation of roughness produced by Graham-Brown's æsthesiometer. This instrument with its graduated projection is peculiarly liable to cause an unpleasant sensation, and occasionally confusion is produced because even the smooth surface of the instrument may evoke a widespread tingling. But in most cases it is easy to show that the threshold for the appreciation of roughness as measured with this instrument is the same on the two halves of the body.

(k) Summary of the Loss of Sensation.

We can now sum up the forms assumed by the loss of sensation which may be found in these cases.

No sensory functions are so frequently affected as the appreciation of posture and the recognition of passive movement. The amount of this loss varies greatly from a scarcely measurable defect to complete want of recognition of the posture of the limbs on the abnormal half of the body.

Tactile sensibility is frequently diminished; but, excepting in a few cases where all appreciation of contact was destroyed, a threshold could be obtained. It was always possible to show that increasing the strength of the stimulus improved the proportion of right answers unless the observations were confused by the disagreeable tingling or other accessory sensations.

Localization of the spot touched was defective in half the cases where sensation was sufficiently preserved to carry out accurate tests. This inability to recognize the site of stimulation was equally great, whether the patient was pricked or touched. In cases where localization was gravely affected, the disagreeable sensation, so easily evoked, tended to spread widely on the abnormal half of the body. A prick on the hand may cause an extremely painful sensation in the cheek or side, and sometimes the patient simply recognized the stimulus as a change within himself, and did not refer the discomfort from which he suffered to the action of any external agent.

Sensibility to heat and cold may show all degrees of change from total loss to a slight increase of the neutral zone. Heat and cold are not dissociated; and if one form of sensation is lost, the other will be gravely disturbed. The apparent exceptions arise from a misinterpretation of the sensation evoked by high or low temperatures on the affected half of the body.

Not infrequently the compass-test cannot be carried out because of the gross loss of sensation and inability to recognize contact; but whenever this method can be applied a threshold can be worked out, and widening the distance between the points increases the accuracy of the answers.

The power of estimating the relation between two weights is frequently disturbed on the abnormal half of the body. If the appreciation of posture and movement is affected, the patient can no longer recognize the identity or the difference of two weights placed in the unsupported hands. But so long as tactile sensibility is not diminished, he can still estimate the relation between weights applied one after the other to the same spot, and can recognize the increase or diminution in weight of an object already resting on the hand.

The appreciation of relative size is often disturbed in these cases, but with care it is usually possible to demonstrate a difference-threshold. Shape and form in three dimensions are frequently not recognizable on the affected hand. But, if tactile sensibility is not grossly affected, the patient usually retains an idea that the object possesses a form, and may obtain a considerable percentage of right answers.

Vibration of the tuning-fork was recognized by all but three of our patients. In almost every case, however, the length of time during which it was appreciated was shorter, and sometimes the rate of vibration was thought to be slower on the affected half of the body.

Roughness, as tested with Graham-Brown's æsthesiometer, was always recognized, except in three cases where the loss of all forms of sensation was extremely severe. Usually the threshold was the same on the two sides, but it was occasionally raised on the affected hand.

CHAPTER III.—SENSORY DISTURBANCES PRODUCED BY LESIONS OF THE CEREBRAL CORTEX.

In describing the effect of a cortical lesion upon sensibility, we shall proceed exactly as with lesions of other parts of the nervous system. Each stimulus will be considered in order and the nature of the response described. Thus, for instance, we shall not speak of "deep sensibility" as preserved or lost, but shall give the exact stimuli used and the form of response they evoked. All such expressions as "cutaneous sensation" and "light touch" will be strictly avoided and we shall deal as far as possible with measured stimuli only.

§ 1.—*Graduated Tactile Stimuli.*

(*Von Frey's Hairs and Pressure-æsthesiometer.*)

Lesions at lower levels of the nervous system produce, on the whole, forms of altered sensibility which react with remarkable constancy to graduated stimuli. A touch of definite intensity, if sufficiently strong to evoke a sensation, will do so in a large proportion of instances; while some less intense stimulus will cause no sensation of any kind. Somewhere between these two we are justified in placing the threshold for tactile sensibility.

But the characteristic change produced by a cortical lesion consists essentially in a want of constancy and uniformity of response to the same tactile stimulus. Increasing the stimulus does not necessarily improve the patient's answers and in many cases no threshold can be obtained.¹

On attempting to obtain a maximum threshold on the affected hand, we meet with the same curious irregularity of response that has hampered all who have attempted to use graduated stimuli in such cases; the patient seems to be untrustworthy. At one time he responds to a hair of 21 grm./mm.², at another even 100 grm./mm.² produces no effect. Not only are his answers apparently incalculable, but not infrequently he responds when he has not been touched.

This irregularity has led most observers to reject all graduated stimuli and to adopt some other form of tactile stimulation, such as rubbing with the finger or with cotton-wool, to which the answers are more uniform. But in this irregular response to graduated tactile stimuli lies the key to the sensory disturbance produced by lesions of the cerebral cortex.

We have modified the method of examination in the following manner so as to bring out the true nature of this phenomenon: A hair is selected producing a stimulus just above the maximum threshold, to which the normal hand reacts with constancy when it is applied sixteen times in the minute. If the same hair is used in the same manner to a corresponding part of the affected hand, the response is irregular and wanting in uniformity. Then more powerful hairs are used, up to those exerting many times the pressure. Still the response remains irregular; in fact, the answers may be less accurate with the more powerful stimulus than with the finer hairs. But further stimulation

¹ Throughout the work we obtain a threshold by finding a stimulus of a strength just sufficient to produce an overwhelming majority of right answers when applied in series. This may be called the Maximum Threshold. We do not attempt to determine the smallest stimulus which can be perceived.

with the hairs of lower grade does not of necessity materially reduce the proportion of correct answers. The irregular response to the more powerful hairs cannot therefore have been due to fatigue alone.

The following series illustrates the nature of this response. The observations began on the normal hand with sixteen touches from a hair of 21 grm./mm.², to which the patient responded promptly in every case. Then the affected hand was touched sixteen times with the same hair and five of these touches were appreciated. A stronger hair was chosen, and eight out of sixteen contacts were appreciated. Step by step the strength of the stimulus was increased, but even with 100 grm./mm.², which exerts a pressure of 3.5 grm., we obtained six responses only. We then decreased the strength of the stimulus again and at the end of the series we obtained a better set of answers to the weakest hair than to the strongest hair previously employed. Finally, on the normal hand all the touches with the lightest hair were promptly recognized, showing that general fatigue played no part in the peculiar form assumed by the response from the affected hand.

	Normal hand (R.)	Affected hand (L.)
21 grm./mm. ²		
21 grm./mm. ²	-----	
23 grm./mm. ²	-----	
35 grm./mm. ²	-----	
100 grm./mm. ²	-----	
23 grm./mm. ²	-----	
21 grm./mm. ²	-----	
21 grm./mm. ²		

To show the record obtained when von Frey's hairs of various bending strains were applied sixteen times in the minute to similar parts of the normal and affected hands. A stroke represents a correct answer, a nought that the patient did not respond.

This record can be translated into the following numbers :—

			Normal hand (R.)		Affected hand (L.)
21 grm./mm. ²	..	..	16 out of 16	..	—
21	„	..	—	..	5 out of 16
23	„	..	—	..	8 „ 16
35	„	..	—	..	6 „ 16
100	„	..	—	..	6 „ 16
23	„	..	—	..	4 „ 16
21	„	..	—	..	7 „ 16
21	„	..	16 out of 16	..	—

It is obvious from these figures that in such a case we can no longer talk of a threshold to von Frey's hairs on the affected hand. For although the hand reacted to 21 grm./mm.² (0.36 grm.) it failed to react in a considerable proportion of instances to 100 grm./mm.² (3.5 grm.). Further stimulation with 21 grm./mm.² produced a larger

proportion of right answers compared with those evoked immediately before by 100 grm./mm.²

Such a result only permits us to say that the range between the minimum stimulus to which the patient responds and the maximum threshold extends between 21 grm./mm.² and something above 100 grm./mm.² We cannot so far say that no threshold exists to measured tactile stimuli. Unfortunately hairs above 100 grm./mm.² are liable to evoke a sensation of pricking on many parts of the normal hand, and it is therefore impossible to employ them without running the risk of introducing a disturbing sensation of pain.

But if a series of graduated pressures are allowed to act upon a stout bristle, which does not bend, it is possible to produce greater tactile stimuli which evoke no sensation of pricking. When this test was applied to the patient who yielded the record on p. 148, we obtained the following results:—

	Normal hand (R.)	Affected hand (L.)
0.2 grm.	○	
0.2 grm.		○ ○ ○○ ○○: ○○○○
0.3 grm.		○ ○○○○○○○ ○○ ○○
0.4 grm.		○○ ○:○○○ ○ ○○ ○○ ○○
0.5 grm.		○ ○○ ○○○○○ ○○○○○○
0.75 grm.		○○○ ○○○○○○○○○ ○
1.0 grm.		○○○ ○ ○ ○ ○○○○○
1.5 grm.		○ ○○ ○ ○:○:○ ○○
2.0 grm.		○ ○○○○○○○ ○ ○○ ○○○
4.0 grm.		○○ ○○○ :○ ○ ○
5.0 grm.		○○○○ ○○ ○○ ○
1.0 grm.		○○ ○○○○○ ○○○○○○ ○
0.2 grm.		

The figures in the first column represent the weight in grammes acting on a constant surface of 0.19 mm.² As before, a stroke represents a correct answer, a nought signifies that the patient did not reply. A dotted stroke represents a hallucination.

This record can be translated into the following numbers:—

	Normal hand (R.)				Affected hand (L.)			
0.2 grm.	..	..	15 out of 16	..	..	—		
0.2 „	..	..	..	..	..	6 out of 16		
0.3 „	..	..	..	..	..	5 „	16	
0.4 „	..	..	..	..	..	5 „	16	
0.5 „	..	..	..	..	..	4 „	16	
0.75 „	..	..	..	..	..	4 „	16	
1.0 „	..	..	..	..	..	6 „	16	
1.5 „	..	..	..	..	..	7 „	16	
2.0 „	..	..	..	..	..	4 „	16	
4.0 „	..	..	..	..	..	9 „	16	
5.0 „	..	..	..	..	..	8 „	16	
1.0 „	..	..	..	..	..	3 „	16	
0.2 „	..	..	16 out of 16	..	..	—		

These observations show that, in this patient, a stronger tactile stimulus did not of necessity lead to a corresponding increase in the proportion of right answers.

Even more striking evidence of the absence of a tactile threshold was obtained in Case 15 with the pressure-æsthesiometer, an instrument by which measured weights may be brought to bear on a surface of

	Normal hand (R.)	Affected hand (L.)
2 gm.		
2 gm.		O O O O O O O O O O O O O
5 gm.		O O O O O O O O O O O O O O
12 gm.		O O O O O O O O O O O O O
32 gm.		O O O O O O O O O O O O O O
2 gm.		O O O O O O O O O O O O O O O O
7 gm.		O O O O O O O O O O O O O O O
12 gm.		O O O O O O O O O O O O O O O O
22 gm.		O O O O O O O O O O O O O O O
32 gm.		O O O O O O O O O O O O O O O
2 gm.		O O O O O O O O O O
2 gm.		

A set of observations obtained in Case 15 to contacts with the pressure-æsthesiometer. In the first column is given the weight acting on a surface 3 mm. in diameter for each series of sixteen tactile stimuli. The symbols used to record the answers are the same as in previous figures. They can be translated as follows:—

PRESSURE-ÆSTHESIOMETER.

	Normal hand				Affected hand			
2 gm.	..	..	16 out of 16	..	..	..	..	..
2 "	..	..	..	..	..	2 out of 16	..	..
5 "	..	..	..	..	..	0 "	16	..
12 "	..	..	..	..	..	4 "	16	..
32 "	..	..	..	..	..	6 "	16	..
2 "	..	..	..	..	..	0 "	16	..
7 "	..	..	..	..	..	2 "	16	..
12 "	..	..	..	..	..	2 "	16	..
22 "	..	..	..	..	..	1 "	16	..
32 "	..	..	..	..	..	1 "	16	..
2 "	..	..	..	..	..	6 "	16	..
2 "	..	..	16 out of 16	..	..	..	..	..

3 mm. in diameter. To contact with this apparatus the normal hand responded constantly. But on the abnormal hand the answers showed the same remarkable tendency to irregularity that was present when it was stimulated with graduated hairs. No pressure between 2 gm.—the minimum weight of the instrument—and 32 gm. seemed to make any constant difference in the number of right answers. In the above

series the best set of answers occurred with 32 grm., but this was equalled by the final series obtained with 2 grm. And yet at the same time the part was not insensitive to tactile stimuli, for with a hair which exerted a pressure of 0.36 grm. (21 grm./mm.²) nine out of sixteen touches were appreciated (*vide* Appendix II, p. 242).

Here, then, it is impossible to say that any tactile threshold can be obtained in the sense usually given to the term. A part that was sensitive to a hair exerting a pressure of 0.36 grm. was not constantly sensitive to a pressure of 32 grm.

This uncertainty of response is not the only peculiarity met with in examining the affected part with measured tactile stimuli. Fatigue is induced with unusual facility and a part that has responded in the characteristic manner to one of the less powerful hairs may cease altogether to respond to 100 grm./mm.² This is, however, an extreme reaction seldom, if ever, seen in uncomplicated cortical cases.

Another disturbing factor in the response to graduated tactile stimuli is the occurrence of hallucinations, or replies that are not the direct sequel to a stimulus. We believe that this tendency to hallucinate is not due to any general untrustworthiness on the part of the patient, but is another aspect of the irregular response characteristic of cortical loss. On one occasion Hn. (Case 14) gave so many hallucinatory answers to graduated hair-stimulation of the affected hand that all testing became impossible. But in spite of this "untrustworthiness" the answers obtained from the normal hand and from the soles of both feet were excellent, and on all these parts a perfect threshold could be worked out.

Many of our patients are highly intelligent; if they are asked to describe their sensations at the time they are hallucinating, introspection leads them to remarkably similar conclusions. They start by saying that a sensation from the affected part differs from that evoked by the same stimulus on the normal hand or foot. The hair seems to remain in contact with the skin, and after a series of touches a continuous sensation is produced. Upon this continuous sensation each consecutive touch may or may not produce that additional change recognized as a fresh contact. But at times the sensation interpreted as another contact may arise without actual stimulation and sometimes it may even recur several times.

These hallucinations are in fact the direct consequence of that persistence of sensation, so frequently a feature of the changes produced by a cortical lesion.

Frequently, however, tactile sensibility is less grossly affected by a cortical lesion. The response may still be irregular and the sensation of contact may persist; but with stronger stimuli the proportion of replies increases until, perhaps, every contact may evoke an answer. Under such circumstances, the affected part may exhibit unusual signs of fatigue, although general attention, shown by the response on the normal side, has undergone no diminution (Case 14, p. 237). Moreover, the sensations of contact tend to persist and hallucinations may break an otherwise perfect series of replies.

Whenever a tactile threshold can be obtained, sensibility as a whole is comparatively slightly affected. No form of sensory appreciation is completely lost and some approximation to a threshold can be discovered with other graduated tests, such as the compasses.

The defects revealed by graduated tactile stimuli are less evident on testing with a camel's hair brush or by moving a wisp of cotton-wool backwards and forwards over the affected part.¹ If it happens to be endowed with hairs, there may be no difference between the constancy of the patient's answers from the two sides, but over hairless parts or after removal of the hairs the replies to cotton-wool stimulation are usually less certain and more irregular than over similar normal areas. Moreover, the patient sometimes complains that the touch of the cotton-wool is "less plain" over the affected limb; but not infrequently he says he can appreciate no difference. Changes that are evident to tests with graduated hairs may be less manifest on stimulation with cotton-wool. This is due in part to the fact that movement of cotton-wool over hair-clad parts evokes a tickling sensation different in nature and origin from the single contact of a measured tactile stimulus (*vide* p. 133).

We can sum up the conclusions to which we have arrived as follows:—

(1) A cortical lesion may reduce the accuracy of response, from the affected part, to graduated tactile stimuli.

The form assumed by this defective sensibility differs from that produced by lesions at other levels of the nervous system. For the affected part may respond to the same graduated hair as the normal

¹ Movement over the surface greatly increases the effect of any stimulus such as cotton-wool. For, firstly, the area affected is greater than if the cotton-wool were simply brought into contact with the skin. Secondly, the leverage of the hairs set in motion by dragging a wisp of cotton-wool or a brush across the part greatly increases the stimulating effect. Finally, movement across the surface is in itself a powerful stimulus, and, as we have shown when discussing the results of lesions of the optic thalamus, may evoke a sensation although simple contact is not appreciated.

hand; but this response is irregular and uncertain. Increasing the stimulus may lead to no corresponding improvement, and even the strongest tactile hair may occasionally evoke less certain answers than a hair of much smaller bending strain. Moreover, a touch with the unweighted æsthesiometer may be as effective at one moment as the same instrument weighted with 30 grm. at another. In such cases no tactile threshold can be any longer obtained.

(2) This irregularity of response is associated with persistence of the tactile sensation and a tendency to hallucinations of touch.

Where the sensory defect is not sufficiently gross to abolish the threshold, persistence, irregularity of response and a tendency to hallucinate may still disturb the records.

(3) In all cases where tactile sensibility is affected, whether a threshold can be obtained or not, fatigue is induced with unusual facility. Although the patient may cease to respond to tactile stimuli over the affected part in consequence of fatigue, his answers may remain as good as before from the normal parts. The fatigue is local and not general.

(4) With stationary cortical lesions, uncomplicated by states of shock or by "diaschisis," sensibility to touches with cotton-wool is never lost over hair-clad parts. Over hairless parts stimulation with cotton-wool may produce a sensation which seems "less plain" to the patient, and his answers may show the same inconstancy so evident when he is tested with graduated tactile stimuli.

§ 2.—*Measured Painful Stimuli.*

In all lesions of the sensory path below the optic thalamus, some loss of sensation to painful stimuli is of common occurrence. But we have never discovered any disturbance of this form of sensibility as the consequence of a stationary cortical lesion, except when the disease was of recent origin or unless the patient had suffered shortly before from convulsions, or had been subjected to other causes of shock.

A prick is the only effective means of applying a measurable painful stimulus to the skin. But all mechanical means for measuring the force needed to evoke a sensation of pain, when a sharp point is thrust into the skin, labour under the same disadvantage. Any sharp object, such as a needle, produces first of all the recognition that the stimulus is pointed: further pressure adds to this a sensation of pain. Now, it is almost impossible to prevent the ordinary patient from saying that he

is pricked whenever he appreciates that the stimulus is a sharp point and if he is told to wait until he obtains a sensation of pain we run the risk of placing the threshold too high.

Usually the patient can discover no difference between two pricks of the same force applied to similar portions on the two sides of the body, but occasionally he states that the stimulus is "plainer" or "sharper" on the normal than on the abnormal part.

This difference in sensation is accompanied by no raising of the threshold either to prick or to painful pressure. The readings obtained with the prick-algesimeter, or with the pressure-algometer, are the same on the two sides. Moreover, the patient shows no more signs of discomfort from the one side than from the other, with the same stimulus.

We therefore believe that this want of "plainness," or "sharpness," of which the patient may complain, is due to a want of distinct appreciation of the pointed nature of the stimulus; that is to say, the want of "plainness" or "sharpness" is not due to a diminished sensibility to the painful aspect of the prick, but is a discriminative loss equivalent to the want of recognition of size and shape (cf. Case 15, p. 242).

The pressure-algometer gives a measure of discomfort rather than pain. To this coarse stimulus the affected part responds as readily as the normal and we have found none of that over-reaction so prominent a feature with lesions of the optic thalamus.

Thus, pure cortical lesions cause no increase or decrease of sensibility to measured painful stimuli. But, if the cortical destruction is recent or progressive, or if it produces convulsions, however slight, remarkable defects may appear in painful sensibility. The threshold, not only to prick but to painful pressure, may be considerably raised, and sometimes even coarse pricking may fail to evoke a sensation with any certainty. In fact, we may be face to face with a truly diminished sensibility to painful stimuli closely resembling the loss produced by interference with sensory impulses at a lower level. These changes are due to shock, exhaustion, and to the state called by Monakow "diaschisis." They are due to a profound disturbance of function, extending back beyond the level of the sensory cortex and affecting even the receptive mechanism in the optic thalamus.

In conclusion, a pure cortical lesion leads to no change in the threshold to measurable painful or uncomfortable stimuli. Nor does the patient express greater dislike to these stimuli on one side than on the other. A prick may be said to be "plainer" or "sharper" on the

normal than on the affected side; but this is due to a defective appreciation of the pointed nature of the stimulus and bears no direct relation to the painfulness of the sensation evoked.

§ 3.—*Temperature.*

Many cortical lesions produce no change in the response to thermal stimuli, provided those periods of shock, which follow an operation or an epileptiform seizure, are strictly avoided.

In other cases, however, we found definite changes in the sensibility of the affected parts to heat and cold, although the lesion had remained quiescent for many years (Case 15 and Case 16). In every case the nature of the disturbance of sensation was similar and consisted essentially in an increase of the range within which a thermal stimulus was thought to be neither hot nor cold.

Normally this neutral zone varies greatly under different conditions and in different persons. It usually occupies from 2° to 5° C., but its position on the scale shifts with the external temperature. At any moment it can be raised or lowered by warming or cooling the hand; but, although the position on the scale may be shifted by adaptation, the interval in which a thermal stimulus is thought to be neither hot nor cold is not materially altered.

Fortunately, in all our cases we were able to compare the behaviour of the normal and the affected sides of the body under the same conditions and with equal care. Now, wherever the appreciation of thermal stimuli was affected by a cortical lesion, this neutral zone extended over a greater number of degrees than on the normal hand. In one instance (Case 15) it lay between 29° C. and 31° C. for the normal hand, whilst on the affected hand all temperatures between 27° C. and 36° C. seemed to be neither hot nor cold. In another patient this neutral zone extended from 23° C. to 38° C. on the affected side.

Not only is the range of the neutral zone increased, but the responses from the affected hand are slow and irregular compared with those obtained from normal parts under similar conditions. The patients complained that heat and cold, which they could recognize correctly, seemed "less plain" over the abnormal than over similar normal parts; they were conscious that even temperatures which they could appreciate produced a different effect upon the two sides.

Moreover the power of comparing two thermal stimuli, applied either together or in sequence, may be diminished. Temperatures of 40° C. and 48° C. may be correctly appreciated throughout a long series of

tests; yet the patient may be unable to say with any certainty which is the hotter. He is puzzled by the inconstant intensity of the sensation evoked by the same temperature at different times. He may have no doubt that tubes containing melting ice and water at 20° C. are both cold, but he cannot tell, with any approach to certainty, which of the two is the colder.

Here, as with the defects in tactile sensibility, it is the power of discrimination, the faculty of comparing two stimuli with one another, which is disturbed by a cortical lesion. The only actual loss of sensation, therefore, falls upon that part of the scale where thermal recognition habitually depends on some previously existing standard. In a normal person anything which alters this standard, such as warming or cooling the hand, may even change the name given to a particular temperature in the neighbourhood of this neutral zone; 30° C. can seem at one time warm, at another cold, and on the third occasion neutral. Cortical lesions therefore enlarge this neutral zone and all thermal sensibility is abolished over that part of the scale where the appreciation of heat and cold depends upon the relation to some pre-existent standard.

Shock or convulsive attacks may produce profound loss of sensibility, corresponding more nearly with the changes which follow lesions at lower levels of the nervous system; but such gross sensory defects never result from quiescent lesions confined to the cerebral cortex.

In conclusion, we find that the appreciation of heat and cold was not affected in a considerable number of cases of cortical lesions. But whenever thermal sensibility was disturbed the following changes were found:—

(1) The neutral zone, within which the stimulus was said to be neither hot nor cold, was considerably enlarged in comparison with that observed on similar normal parts of the same patient.

(2) The patient complained that, although he recognized correctly the nature of the stimulus, it seemed "less plain" than over normal parts. His answers were less constant and less certain; a temperature recognized without difficulty at one time seemed doubtful at another.

(3) The power of discriminating the relative coolness of two cold stimuli, or the relative warmth of two hot tubes may be diminished. Thus 20° C. may be said to be the same as ice, although both are uniformly called cold, and 40° C. may seem as warm as or even warmer than 48° C. The faculty of appreciating the relation to one another of two temperatures on the same side of the scale is disturbed.

§ 4.—*The Appreciation of Posture and of Passive Movement.*

Inability to recognize the position of the affected part in space is the most frequent sensory defect produced by lesions of the cerebral cortex. In some cases, this and the allied faculty of recognizing passive movement may be the only discoverable abnormalities. Whenever sensation is disturbed at all, these two forms of spacial recognition will be certainly affected.

Since some disturbance of the power of recognizing passive movement always accompanies defective postural recognition, these two kindred faculties will be dealt with together in this section.

(a) *Recognition of Posture.*

In most cases of cortical disease, the usual rough method of testing is amply sufficient to demonstrate defective appreciation of posture. The patient's eyes are closed and the affected limb is placed in some position different from that in which it lay at first. He is then told to touch some part of it, such as the index-finger, with his normal hand. At first he usually fails to find the limb; when at last he strikes some part of it, he moves his indicating hand down to find the finger he was asked to touch. Should the power of localization remain intact, he can ultimately grope his way to the exact spot; but, if localization is also affected, although he may reach the hand, he will probably be unable to find the finger.

So gross is the defective recognition of posture in most cases that this method amply suffices to demonstrate it in an unequivocal manner. Horsley [14] has, however, introduced a useful means of measuring this deviation from the normal.

The finger to be tested is applied to the one surface of a glass plate divided by lines into measured squares, and with the free hand the patient seeks to indicate on the other surface of the plate the position of the finger he is seeking. The results of his attempts can be read off on the measured plate. Instead of this glass plate we have used a piece of stiff cardboard. In the centre of the one surface of this cardboard is a slight depression to receive the tip of the index-finger, and on the other a sheet of white paper can be fixed. With the normal hand the patient seeks to indicate the position of the affected finger, which remains at rest in the depression, and the point upon which he ultimately settles is marked on the paper. His indicating hand is then withdrawn

and he is asked to make another attempt. Each record of a series of observations made in this way can be measured and collated at leisure.

In every case where sensation was disturbed in any way, however slightly, as the result of a cortical lesion, the records with Horsley's plate showed some loss of postural appreciation in the affected hand. This method therefore forms a delicate means of detecting sensory changes of cortical origin.

Thus in Case 14 we obtained the following results with the plate horizontal at the umbilical level: Four attempts only out of ten came within 7 cm. of the affected index. When the plate was held in the sagittal plane, two attempts to find the index of the affected hand fell within 4 cm. of its position and a circle with a radius of 8 cm. was required to cover the remaining eight points.

The deviations discovered by Horsley's method, even in normal individuals, are so considerable that it is necessary to have some standard in each patient with which to compare the records obtained from the affected parts. It might be objected that most cortical lesions produce so much paralysis that the affected hand cannot be used to point out the position of the normal forefinger. But, in spite of its paresis and defective sense of posture, the records obtained when the affected hand sought the normal forefinger were uniformly better than when the patient attempted to point to the affected forefinger with his normal hand. That is to say, defective appreciation of the position of the hand to be sought for has a more disturbing effect upon the records than weakness and loss of postural sense in the indicating hand.

This is particularly well shown by the records from a patient in whom the left hand was gravely paretic, and the sense of posture defective: and yet all ten attempts with this hand to find the normal forefinger fell within 3 cm. of its position, and five lay within a distance of 1 cm. But when he attempted to point to the affected index with the normal hand he came once only within a distance of 1 cm. and three attempts lay outside a radius of 3 cm. Thus the normal hand seeking the affected forefinger made a worse record than the abnormal hand attempting to find the normal index, whose position was known.¹

All these tests depend on knowledge of the position in space of the

¹ The most important postural impulses for the act of pointing are those from the shoulder joint and, in these limited lesions of the cortex, the shoulder is usually less affected than the distal segments of the upper extremity. Thus, even a gravely paralysed limb can often be guided more correctly in the desired direction than the normal limb attempting to point to a spot of which the position is imperfectly known.

extremity as a whole. To what extent its separate segments are affected can only be discovered by asking the patient to imitate, as exactly as possible with his normal limb, the posture of the affected part. His eyes are closed and, whilst his attention is diverted by conversation, some part such as the index-finger is moved into the desired position. After an interval he is asked to place his normal index in the same position as the index of the opposite hand. By this means we have been able to confirm the statements of most recent writers that the gravest loss produced by a cortical lesion is usually found in the extremity of the limb (Goldscheider [10], Petrén, Bergmark [1]).

(b) Recognition of Passive Movement.

The inability to recognize posture is always associated with diminished appreciation of passive movements, in some cases so great that even complete flexion and extension of a joint cannot be recognized. Here no measurement is required; the loss of appreciation is absolute. But whenever the loss is less gross we agree with Petrén and his fellow-workers that the smallest movement which can be appreciated by the patient must be measured: such measurement alone can demonstrate whether this faculty is or is not affected.

Measurements alone can furnish us with the materials for determining the relative extent to which the appreciation of passive movement is disturbed at the various joints of the affected limb, and in cases where the condition of the patient is changing, they may form a useful record of the progress of the disease.

But when we attempt to measure the extent of the smallest appreciable movement, two different phases of recognition must be distinguished. The patient may say at once when he thinks a movement has occurred; this gives the measure of the least perceptible movement. Or he may wait until he is able to indicate its direction. As a rule in the normal limb, most patients wait until they can recognize the direction of the movement before they say that the joint has been moved; but the difference between the point at which the movement is appreciated and that at which its direction is recognized is normally small.

In the abnormal limb, however, this distance is greatly exaggerated and movements may be perceived long before their direction can be recognized. It is, therefore, important to record both the extent of the smallest movement perceived and the range necessary to evoke recognition of its direction.

All these points are well shown in the records from a case where

the lesion produced slight sensory changes only; here the power of recognizing passive movements might have been said to be unaffected, had it not been for the measurements. On the normal side the patient waited until he could recognize the direction of the movement, and yet when the little finger was flexed or extended was invariably correct with movements within 5° . On the abnormal side he was never certain of the direction of the movement until it had exceeded 10° , although he frequently appreciated the occurrence of a movement of 5° .

All cortical lesions, which produce any change in sensibility, lessen the power of appreciating passive movements and the knowledge of their direction. In every case this loss was associated with a concomitant disturbance of the recognition of posture. Whenever sensibility was changed, however slightly, these two allied functions were always affected. Diminished power of appreciating the posture of some part of the limb, and of recognizing passive movements, are the most constant and most easily demonstrable defects of sensation produced by cortical lesions.

In all our cases the loss was greatest towards the distal portions of the limb; in this it corresponds exactly with the disturbance of the sense of posture. Here we can only confirm the work of almost every previous observer.

When attempting to measure the smallest appreciable movement we have been struck with the tendency to inconstant answers when testing the affected limbs. On the normal side most patients are remarkably constant and the values obtained often do not vary by one degree. Thus when the normal elbow was flexed or extended in one case all the answers lay between 1.5° and 2.5° . But with movements at the affected elbow the answers ranged between 10° and 22° .

Another striking phenomenon in these cases is the occurrence of hallucinations of movement. Even though the limb remains at rest the patient may describe sensations of movement which seem to him as clear as those evoked by our manipulations.

In conclusion, we find, like most of our predecessors, that—

(1) Cortical lesions most frequently disturb the recognition of posture and of passive movements. Whenever sensation is in any way affected in consequence of a cortical lesion these two functions suffer.

(2) In all our cases the disturbance in the faculty of recognizing posture and passive movements was greater towards the peripheral parts of the affected limb.

(3) When a patient with unilateral disturbance of these faculties attempts to point to some part of his body, defective knowledge of its position causes greater error than want of recognition of posture and movement in the hand with which he points.

(4) When testing the patient's power of appreciating passive movement, the answers are frequently uncertain and hallucinations of movement may occur. And yet the patient may be remarkably consistent and accurate when normal parts are tested.

§ 5.—*Localization.*

By localization we understand the power of recognizing correctly the spot that has been stimulated, and it would seem, at first sight, that little difficulty could arise in discovering whether this faculty was affected or not; but a good deal of confusion exists owing to technical difficulties inherent in the methods usually employed to investigate the power of localization. (*Vide* Appendix I, p. 199.)

Of all the methods at present in use that of Henri is probably the most suitable. Excellent and simple as we found this method, it labours under one serious defect for clinical purposes. Some of our patients were liable to become confused when asked to point out the spot stimulated on a diagram, picture, or even on a photograph of the hand. We therefore adopted the following modification, which we found to be a great improvement on the original Henri method.

The hand to be tested, for example the left, is hidden from the patient's sight with a screen. One of us standing behind places his own left hand in a similar position in full view of the patient, who indicates on this living model the situation of the place where he believes he has been touched. A second observer marks on a life-sized diagram the position of the stimulated spot and the point indicated by the patient. This method we have employed throughout this work. It avoids both the technical difficulties of spot-naming and the fallacies of the groping method, and is peculiarly useful in clinical investigations.

The uncertainty and irregularity of response to tactile and pressure stimuli, so common a consequence of cortical lesions, is liable to lead to fallacious results when testing the power of localization. We usually, therefore, touch the spot with some blunt instrument of neutral temperature, and continue the touches until the patient says he appreciates the contact. He then indicates on the hand of one of the observers the situation of the stimulated spot.

Were we concerned with a cutaneous sensory loss consequent on a lesion of peripheral nerves this method would be fallacious, for such touches stimulate the afferent mechanism of deep sensibility. But tactile impulses evoked from the skin and those which pass by way of the deep afferent system have united into a single tactile group long before they reach the optic thalamus. We are, therefore, justified in using any form of tactile stimulus which the patient can appreciate, in order to test his power of localization.

The power of recognizing the position of a spot stimulated is comparatively seldom affected as a consequence of pure cortical lesions, provided all periods of shock are avoided. Most seizures, and all operations on the brain, are followed by temporary loss of this function, grossly in excess of anything found with stationary lesions of the cortex.

The methods we have employed enable us to discover whether the power of localization is intact or not, although the patient is entirely ignorant of the position of the affected limb; it may be, even under these conditions, that every part of the affected hand can be touched in succession without a single mistaken answer. But, should localization be affected, scarcely a single stimulus is referred to its correct position and the patient frequently complains that he has "no idea" where he has been touched.

Some observers (Horsley and Russel [37]) have stated that, when localization is disturbed by lesions of the cortex, the position of the indicated spot lies in some constant relation to that of the point stimulated. Our failure to discover any uniform tendency to erroneous localization in one direction is probably due to the method we have adopted, and particularly to the avoidance of groping.¹ The dual and composite nature of the groping method is well shown by the effect produced by moving the hand; movements of which the patient is unconscious may cause a fundamental change in the direction towards which he tends to localize, if he is allowed to grope for the spot touched. Thus proximal can be converted into distal localization by drawing the hand nearer the body, and a preponderating tendency to localize in a postaxial direction can be converted into a pre-axial direction by turning over the hand. Suppose that, when testing the dorsum, the majority of the points indicated lie towards the ulnar

¹ If the power of localization is tested in this way, the patient will usually tend to place his finger on a point proximal to the stimulated spot. But this is due to defective recognition of the position of the limb in space and to the consequent tendency for its distal segments to seem closer to the trunk than is in reality the case. The same "shortening" is present in many cases of phantom limbs following amputation.

side of the stimulated spots; reverse the hand and the larger number will now lie to the radial side. These apparently inconsequent results depend upon the dual nature of the groping test and disappear entirely with the methods we have used.

Moreover, by our methods we obtain records which can be studied at leisure, and the number of observations permanently recorded is sufficient to indicate whether the errors in any direction are due to chance or to a constant displacement of locality.

We cannot insist too strongly that, when localization is defective from lesions of the cortex, the stimulus is not localized in some false direction, but the patient has a vague and uncertain idea amounting in some cases to complete ignorance of its position.

In one case localization was disturbed in the left hand in consequence of removal of a portion of the cortex five years ago (Case 15). On the normal hand, every touch was correctly localized, but on the abnormal hand, out of thirty-three tactile stimuli six only were correctly placed. Eleven were thought to be proximal and eight distal to the spot touched; six were localized falsely over parts of the same level, and in two cases he said he had no idea of the situation of the touch.

Thus the following records were recently obtained from a man in whom a portion of the cortex had been removed from the left hemisphere in 1904 (Case 17). The localization of fifty-six tactile stimuli on each hand could be classified as follows:—

	Correct	Proximal	Distal	Same level	"Don't know"
Normal hand (L.) ..	48	4	2	7	0
Affected hand (R.) ..	14	5	13	14	10

Erroneous localization is not due to the uncertainty in tactile appreciation so commonly produced by a cortical lesion; for it is equally manifest when the stimulus that the patient is asked to localize is a prick about which he is never in doubt. The following observations were made by asking one of our patients with defective localization to indicate the position of a series of pricks:—

	Correct	Proximal	Distal	Same level	"Don't know"
Normal hand (R.) ...	20	0	0	0	0
Abnormal hand (L.) ..	5	6	6	3	0

Defective localization is not a necessary concomitant of the defective recognition of posture so commonly produced by cortical lesions. In several cases where the appreciation of position and passive movement

was gravely affected localization was demonstrated to be perfect by every method except that of groping for the stimulated spot.

For instance, in the case where a small portion of the cortex was removed in 1908 the appreciation of position and passive movement was gravely affected (Case 14). But from observations made on many occasions during the last three years we were unable to find any difference between the power of localization on the two hands, provided the groping method was avoided. He was equally correct whether we used the original or the modified Henri method. He preferred, however, the latter; it seemed to him easier and his answers were more quick and certain.

Moreover, in these cases where the sense of position is gravely defective but localization is good, changing the position of the limb passively does not diminish the accuracy with which the point of stimulation is indicated, provided the groping method is avoided. If a series of readings are taken in the usual way, and, whilst the affected hand still remains screened from sight, its position is changed, subsequent readings are no less accurate than the first series. We can therefore state definitely that the power of recognizing the position of the limbs can be gravely affected as a consequence of cortical lesions without disturbing the accuracy of localization.

The faculty of localizing the stimulated spot as determined by all methods except groping is less often affected by a cortical lesion than the power of appreciating posture. In fact, we have not yet seen a case in which localization was disturbed without a coincident loss in postural recognition.

The conclusions to which we have arrived in this Section may be summed up as follows:—

- (1) The power of localizing the stimulated spot is not infrequently preserved, although sensation may be otherwise disturbed as a consequence of cortical lesions.

- (2) This faculty is independent of the power of recognizing the position of the affected limb; appreciation of posture may be lost, although localization is not in any way diminished.

- (3) If the power of localization is lost, the patient will be unable to recognize not only the position of a spot touched but also the position of a prick.

- (4) When localization is defective in consequence of cerebral lesions, the patient does not habitually localize in any particular direction, but ceases to be certain where he has been touched or pricked.

§ 6.—*The Compass-test.*

Loss of the power to distinguish two points applied to the skin simultaneously is one of the most striking changes produced by cortical lesions. It is not present in every case; the patient may have difficulty in recognizing the posture of the affected limb, and the appreciation of passive movements may be diminished, yet the compass-test may yield equally good results on the two sides.

But with the larger number of cortical lesions the discrimination of two points will be affected. It may be, in the milder cases, that the threshold is raised; to these we shall return later. More commonly no threshold can be obtained even by separating the limbs of the compasses to the widest extent possible within the limits of the principal segments of the affected limb. If a bad record is obtained when the points are 5 cm. apart, widening the distance to 20 cm. may cause no material improvement. Decreasing the difficulty of the problem does not of necessity improve the accuracy of response; determination of a threshold has become impossible.

Any defect in tactile sensibility is liable to disturb the compass-records. When, therefore, we consider the peculiar changes described in the first section of this chapter, the loss in discrimination of two points might appear at first sight to be due to diminished tactile acuity. This cannot, however, be the cause of the defective compass-records; for the inability to distinguish two points applied simultaneously is equally definite if each limb of the compasses is armed with a needle and two pricks replace the two tactile stimuli.

We have already seen that the recognition of a prick is never destroyed in consequence of a cortical lesion, and sensibility to pain undergoes no changes analogous to those of tactile sensibility. It is therefore obvious that the power of recognizing "two-ness" is a separate function of sensation which may be destroyed by a cortical lesion. This loss is not dependent on the changes in tactile sensibility, though the two defects are strictly analogous phenomena.

The response to graduated tactile stimuli is irregular and uncertain. The patient responds intermittently to a stimulus of low intensity, but increasing the stimulus does not necessarily increase the proportion of right answers. An exactly similar change is revealed by the compass-test. All recognition of the double nature of the stimulus may be lost, and it does not matter whether the two points are sharp or blunt. All estimation of a threshold has become impossible, not because the patient is insensitive to the contact of the two points but because the faculty of

distinguishing them has been destroyed by the cortical lesion. This is exactly analogous to the impossibility of obtaining a tactile threshold, and the two phenomena co-exist in most cases.

Not every cortical lesion produces so severe a loss of compass-discrimination. Although the recognition of posture is disturbed, the compass-records may remain equally good on the two sides; but as soon as tactile sensibility shows any of the changes produced by a lesion of the cortex the power of distinguishing two points will also suffer.

Sometimes, in cases where sensation is little disturbed, it is possible by widening the distance between the compass-points to obtain a perfect record over the affected part; a true threshold can then be discovered. But the records tend to be confused by the same irregularity and uncertainty of response so characteristic of the disturbed tactile sensibility in these cases of cortical disease.

Weber's test consists in applying the two points strictly at the same moment. We have already seen that, when this test is affected by lesions at lower levels of the nervous system, the patient can still recognize the double nature of the stimulus if one point is applied to the skin even a fraction of a second after the other. From their origin at the periphery, the impulses which underlie the appreciation of two points applied successively, run separately from those by which we are able to recognize the simultaneous application of the compasses.

But, in a certain proportion of cortical cases, it does not matter whether the compasses are applied simultaneously, or whether an interval is allowed to elapse before the second point touches the skin. The power of recognizing the double nature of the stimulus is lost, and no increase of the distance between the two points makes a constant or material difference to the accuracy of the answers. If the interval is greatly prolonged between the moments at which the first point and the second point touch the surface, the patient generally answers "one" to each application. That is to say, he fails to recognize with any certainty that two points are in contact with his skin, although he perceives each touch separately. Evidently he has lost that faculty by which "two-ness" is recognized, and it does not matter whether the points are applied simultaneously or successively.

Now, whenever successive application of the two points is recognized, localization will be found to be intact. The power of appreciating two points applied successively is in reality the faculty of localizing two spots that have been stimulated one after the other. It is independent of the power of discriminating two stimuli which act upon the surface at the same moment.

This difference was clearly shown in a series of observations made in Case 14. We found that the patient could not recognize two points separated by 3 cm. applied transversely across the back of the hand or fingers. Localization was, however, perfect and he never failed to name correctly the finger that had been touched. The compass-points were then separated to a distance of 2.25 cm., and so applied that each point fell over the basal phalanx of a separate finger. So long as the compasses were applied strictly simultaneously he never said he had been touched on two fingers, but always selected one or the other: he thought he had been stimulated with one point only. But as soon as even a fraction of a second was allowed to elapse between the two contacts he invariably recognized that he had been touched with two points and named the two fingers correctly. The faculty of localization was intact, and he was thereby enabled to appreciate the double contact, provided that the two points did not touch the surface at the same moment.

We may conclude from the observations described in this section that—

(1) A cortical lesion may destroy the power of discriminating two compass-points, both when applied simultaneously and successively.

If this is the case, no threshold can be obtained for either form of the test; increasing the distance between the points does not constantly improve the accuracy of the answers.

(2) This disturbance is not caused by changes in tactile appreciation; for it can be demonstrated equally well with two painful as with two tactile stimuli.

(3) The condition of tactile sensibility and the accuracy of the simultaneous compass-test are closely associated; a disturbance of the tactile threshold is usually accompanied by a raised threshold for the appreciation of two points applied simultaneously.

(4) Should the power be preserved of recognizing two points when the compasses are applied consecutively, localization will be found to be intact. The patient's appreciation of the two points when they are separated by an interval of time is due to the recognition of the separate locality of the two spots touched.

§ 7.—*The Appreciation of Weight.*

This test has been too frequently neglected in clinical work, probably because it demands considerable care on the part of the

observer, and goodwill in the patient. When carefully carried out no test is more satisfactory; for the results can be expressed in a numerical relationship, and when the faculty of recognizing differences in weight is disturbed, the errors, compared with those of the normal hand, are enormous.

There are several ways of conducting this test which are fully described in the chapter on methods (p. 207). But at the highest sensory level, the appreciation of difference in weight depends mainly upon two faculties. When a weight, placed upon the fully supported hand, is either increased or diminished, the recognition of the change is based mainly on the power of appreciating differences in pressure. To estimate the relation between two weights placed upon the hand one after the other requires not only an appreciation of pressure, but the power of relating some consequence of the first weight with the immediate effect of the second weight. Lastly, when a weight is placed at the same moment in each palm, and the patient is allowed to "weigh" the two objects against one another, he relies mainly upon his power of estimating movement and posture.

Cortical lesions usually diminish the accuracy of the answers to all three tests, and, if sensation is severely affected, all power of estimating weight may be lost. Although the patient may still appreciate the contact of the weights that are placed upon his hand, he may be totally unable to recognize their relation to one another, however the test may be applied.

Occasionally, the sensation of something in contact with the hand persists for many seconds after the removal of the weight. But although the patient believes that something still lies in his hand, he cannot estimate its weight in relation to an object on the opposite palm. He says "it is still there, but it does not seem to have any weight."

Conversely, the following condition can be frequently observed. A weight is placed in each hand and allowed to remain there. From time to time the patient is asked to estimate the relation between the two weights. He will almost certainly say that the one in the normal hand is heavier; but gradually he begins to think that there is no weight in the abnormal hand, and the sensations produced by its removal may even be mistaken for the re-application of the weight to the hand. He says, "You have put the weight on again."

In conclusion, we have found that—

(1) The power of estimating the relative weight of two objects of the same size and shape is readily disturbed by cortical lesions.

(2) Though the patient may retain sensations of contact when the weight is placed in his hand, all power of recognizing the relative heaviness of the object has disappeared.

(3) This faculty is equally disturbed in most cases whether the weights are placed on the supported or unsupported hand.

§ 8.—*Appreciation of Size, Shape and Form in Three Dimensions.*

To recognize size, shape and form demands that the relation between two percepts should be correctly appreciated. In the case of the tests for size, we frankly ask our patients for the difference between two objects of the same shape. When testing for shape and form, a relation is always implied between the test-object and something which the patient has experienced before.

In most cases, when sensation is affected, appreciation of size, shape and form in three dimensions is lost; the patient usually complains that he has "not the least idea" of the shape or relative size of the test-objects. Although he insists that he "can feel them quite well," they convey no indication that they possess size, shape, or form. One of our patients recognized that the cone had a point because in his manipulations he pressed it into his hand; but he had no idea that it possessed any shape.

This total abolition of the power to recognize size, shape and form makes the defect peculiarly easy to discover even by the crudest tests. Thus it is universally acknowledged that cortical lesions tend to destroy the power of recognizing common objects, such as a knife, scissors, or coin placed in the hand, and our more accurately graded tests simply serve to confirm this general consensus of opinion.

This defective recognition is not in any way due to the paralysis produced by the cortical destruction; for, in two cases where the movement of the hand was gravely affected, size, shape and form were perfectly recognized. When a test-object is placed in the patient's hand it is of advantage if he can roll it between his fingers; but where the faculty of recognizing these tests is maintained, even objects in three dimensions will be named correctly if the patient's fingers are closed over them passively.

The correct appreciation of size, shape and form does not depend to any great extent on the recognition of posture; for it was perfectly retained in two cases, although postural recognition and the appreciation of passive movement were gravely affected.

But in every case where the sense of posture was affected and we were unable at the same time to obtain a tactile threshold, all recognition of size, shape and form in three dimensions was abolished. Not that such recognition depends directly upon the state of tactile sensibility. The combined affection of the sense of posture and loss of the tactile threshold indicate simply that the defect produced by the lesion has reached a sufficient grade to destroy the power of recognizing identity and difference. The appreciation of size, shape and form, therefore, suffers like all tests which imply a relation.

§ 9.—*Roughness and Texture.*

The power of appreciating roughness can be compared on the two halves of the body by means of the Graham-Brown æsthesiometer. In this instrument one or more cylinders are projected to a measurable extent from a smooth metal surface; and the patient says whether the instrument is smooth or rough when it is moved across some part, such as the hand.

In no case of quiescent cortical lesion was there any appreciable difference between the affected and normal parts. Not only could the patient experience no difference, but the extent to which the cylinder must be protruded to evoke a sensation of roughness was the same for the two sides. This stimulus is one which can be appreciated, notwithstanding grave loss of sensibility produced by a cortical lesion.

But, in spite of this power to recognize the roughness or smoothness of the surface of the æsthesiometer, all appreciation of texture may be lost. This test demands not only the immediate recognition that the object is rough or smooth, but the relation of that sensation to other percepts. Thus, although he may know that one surface is rough and another is smooth, he may be unable to name the substance by its texture. Cotton, silk and stamped velvet are all one to the affected hand, although readily distinguished on the normal side. When once this test has been applied the patients often complain that they have lost all idea of texture, saying, "I can feel it, but I have not the least idea what it is."

These two tests, both depending on the same sensory impulses, clearly illustrate the nature of the loss of sensibility produced by cortical lesions. The one depends upon the immediate appreciation of a smooth or rough stimulus. The other demands the correct relation of one group of percepts to another. The first is therefore maintained, whilst

the second is destroyed by any cortical lesion which produces a measurable disturbance of sensibility.

§ 10.—*Vibration.*

At lower levels of the nervous system, a lesion frequently destroys all power of appreciating the vibrations of a tuning-fork. But we believe this never occurs from a stationary cortical lesion.

Usually the patient can discover no difference in the sensations produced by the fork on the two halves of his body. Occasionally, however, he says it seems "plainer," or "stronger," on the normal than on the affected limb. If this is the case the vibration will be appreciated for a shorter period over the affected parts. The fork is set in motion and the patient is asked to say when he can no longer appreciate the vibration. It is then rapidly transferred to a similar spot on the normal limb and vibration may still be recognized for as much as twenty seconds longer. If this defect were greatly increased it is obvious that the power of recognizing vibration would be abolished; but this never occurs from a pure cortical lesion. The vibration of a tuning-fork seems to contain some sensory element which insures that it is appreciated, even though the cortex is gravely affected. But the cortical lesion diminishes the "plainness" of the sensation and shortens its duration.

In some cases, the vibration of the tuning-fork not only seems "plainer," but is said to beat "faster" on the normal than on the affected limb. As this depends entirely on introspection a few patients only have noticed it, and we have avoided questions which might suggest a difference in apparent rapidity on the two sides.

CHAPTER IV.—ANALYSIS OF THE LOSS OF SENSATION PRODUCED BY LESIONS OF THE OPTIC THALAMUS AND NEIGHBOURING PARTS.

In a previous chapter we have described the various forms of sensation which may be disturbed by lesions of the optic thalamus and its neighbourhood. Test by test we followed the loss of sensation, and showed that it varied in different cases within extreme limits. We shall now attempt to discover by analysis of these disturbances of sensation whether the impulses which pass away from the optic thalamus differ in their grouping from those which enter this organ from the mid-brain.

Since the optic thalamus is the terminal station for all secondary sensory paths, a lesion situated within its limits might destroy the receptive structures in which their impulses end; in such a case the loss of sensation would correspond to that produced by an equivalent lesion of the tracts of the mid-brain by which these impulses are conducted to the optic thalamus.

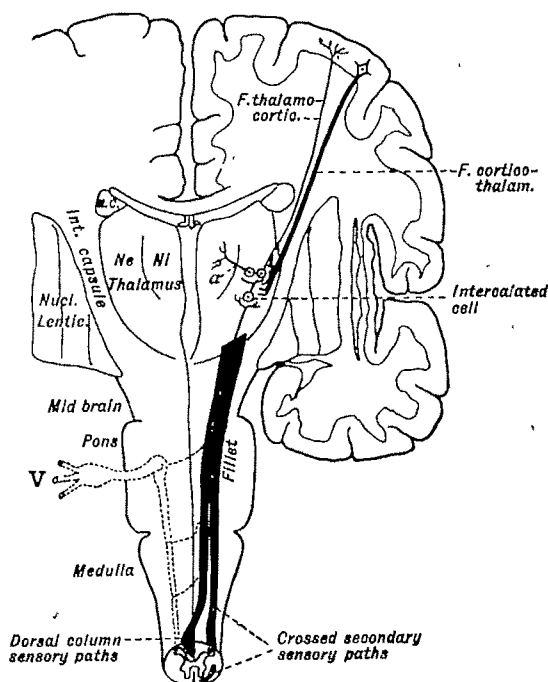


FIG. 4.—To represent diagrammatically the anatomical arrangement of the paths and centres concerned in sensation. Two distinct paths exist in the spinal cord; a crossed secondary path in the ventrolateral column which conveys impressions of pain, temperature and touch, and a second uncrossed path in the dorsal column which also carries touch, and in which run impulses that underlie the sense of position, the appreciation of movement, the discrimination of two points, and the recognition of vibration, size, shape, form, weight and consistence. This second path decussates in the lower part of the medulla oblongata, but runs separate from the first path at least as high as the pons. All these secondary sensory fibres, now crossed, terminate in the ventrolateral region of the optic thalamus. The impressions they carry are regrouped here and, through intercalated neurones, are distributed along two distinct paths; the one carries impressions to the cerebral cortex, the other, we assume, towards the more mesial parts of the optic thalamus. The cortico-thalamic fibres, which terminate in the lateral nucleus of the optic thalamus, are also shown.

On the other hand, the lesion might leave this receptive mechanism intact but interfere with the paths that are streaming away to the cortex. In this case the sensory defect would reveal what elements of

sensation pass to the cortex after they have been regrouped in the thalamus.

In so complex a structure as the thalamus, containing a multitude of incoming and outgoing paths, no lesion could completely destroy one set of impulses only. But, although most cases show evidence of a diffuse disturbance of sensory functions, some point more to partial interference with the receptive mechanism, and some to destruction of the paths which run from the thalamus to the cortex. We shall analyse these two groups separately in order to discover, if possible, the nature of the rearrangement which takes place in the thalamus, and to determine the grouping of the sensory impulses which pass away from this junction to the cortex.

As our object in this paper is to study the nature of the loss of sensation, and not to erect clinical categories for diagnostic purposes, we shall not deal with those cases where a widespread lesion of the optic thalamus abolishes all sensation on one half of the body, and consequently no over-response to affective stimuli is possible.

§ 1.—*Disturbance of the Afferent Receptive Mechanism in the Optic Thalamus.*

In certain cases, which show the over-reaction to afferent stimuli and other signs indicative of a lesion of the optic thalamus, the loss of sensation is extremely gross. Not only is sensibility for touch and temperature abolished, but even the threshold for painful stimuli may be raised. Pain, once appreciated, produces more discomfort on the affected half of the body; but in order that this appreciation may occur, the stimulus must be more intense than on the normal side. The strength of a prick, and the amount of pressure required to produce pain, are greater over the affected parts, although as soon as pain is produced the reaction is excessive. This loss of sensibility is probably due to interference with painful impulses either in the receptive portion of the optic thalamus, or as they still run in the secondary sensory paths which end in this junction.

This conclusion is supported by the extreme loss of other forms of sensation which is found in cases where the pain-threshold is distinctly raised. Moreover, instances have been recorded in the literature where the loss of sensation was of the grossest kind and, although no attempt was made to determine the threshold for various forms of painful stimuli, we have little doubt, from their likeness to cases under our

observation, that the threshold must have been raised. This was the condition in a case described by Roussy, where autopsy revealed a lesion in the neighbourhood of the termination of the fillet.

In one of the cases (Case 6) we have cited in Chapter II sensibility to prick was gravely diminished, and the algometer readings were uniformly higher on the affected half of the body in spite of the profound over-reaction to both stimuli. The patient was entirely insensitive to the thermal element of heat and cold, and showed no discomfort until ice, or water at 60° C., was used; then, however, the response was excessive on the affected half of the body. Even sensibility to the tactile elements of pressure was gravely affected.

Autopsy showed that the caudal portion of the lateral nucleus of the optic thalamus close to the ending of the fillet was the seat of a lesion of vascular origin. In this case a few impulses evoked by stimuli of high intensity could pass the receptive junction of the optic thalamus and excite sensations of pain and discomfort. Had the lesion caused a slightly graver interference with these impulses the loss of sensation would have been absolute, and the characteristic over-response to affective stimuli could not have made its appearance. Roussy ([36], Case 2) has observed an instance of this condition where the patient was insensitive to all stimuli, and the upper end of the fillet within the optic thalamus was found to be involved in the lesion. In such cases the forms assumed by the loss of sensation resemble those produced by a mid-brain lesion; the threshold for touch, for pain, for heat and for cold are much raised, and sensibility to one or more of these stimuli may be abolished entirely.

We believe that in all cases which present the "syndrome thalamique," accompanied by loss of sensation so gross that the threshold is raised to affective stimuli, the receptive mechanism is affected; this seems to be situated mainly in the caudal portion of the lateral nucleus of the optic thalamus.

§ 2.—*Disturbance of Sensory Impulses as they pass from the Optic Thalamus to the Cortex.*

In certain cases which show characteristic signs of a lesion of the optic thalamus, the threshold to prick is identical on the two halves of the body and the readings of the pressure-algometer may be actually lower on the affected side. The loss of appreciation of posture and passive movement may be severe, and the power of comparing two weights may be diminished, but the remaining forms of sensibility are:

less grossly affected than in that group of cases we have just considered in § 1 of this chapter.

Here we believe that the receptive mechanism is not affected to any material extent. The complete retention of painful sensibility shows that the impulses upon which it is based have been allowed to exert their full influence on the central organ where they are transformed into sensation. Moreover, the sensory elements are dissociated in ways which are unknown, until this level is reached; both the nature of the loss of sensation and the character of the sensibility which remains show that the afferent impulses must have been interrupted after they have undergone a fresh regrouping at the thalamic junction. An analysis of these forms of dissociated sensation will therefore show the grouping of the impulses which pass away from the optic thalamus to act upon the sensory cortex.

The first remarkable fact revealed by a study of these cases is that, whenever a stimulus can be appreciated, a threshold can be obtained. The tactile threshold may be raised, but increasing the strength of the measured stimulus improves the accuracy of the answers. In the same way it may be necessary to employ a colder or a warmer tube to evoke a thermal sensation, but, as a rule, a threshold can be obtained without difficulty. Sensibility to any one stimulus tends to be diminished rather than to be abolished completely.

When we turn to the forms assumed by the loss of sensation we find that in every case the recognition of posture and passive movement was more or less gravely disturbed. Sometimes the loss was so slight that it could be discovered by measurement only; but in every case a difference was demonstrable between the two sides. Whenever this loss of appreciation of posture and passive movement exceeded a scarcely perceptible amount, it was accompanied by a diminished power of estimating the difference in weights placed on the unsupported hands.

Tactile sensibility was frequently diminished in these cases, but was never abolished completely. Stronger hairs might be necessary to evoke an answer, but ultimately a threshold could usually be obtained, and increasing the stimulus led to an increase in the accuracy of the responses.

Any material raising of the tactile threshold was accompanied by inability to appreciate the relation of weights placed on the fully supported hand one after the other. Moreover, the patient could no longer recognize with certainty increase or decrease of a weight resting on the affected hand.

Not uncommonly, the simultaneous compass-test was also affected and a threshold could not be obtained until the points had been separated to many times the distance necessary on the normal side. Wherever this test was defective, the power of recognizing size and shape was diminished, showing the probable association at this level of the nervous system of the impulses upon which these various functions depend.

Localization was less often disturbed in the cases at present under consideration; but occasionally the patient had lost the power of indicating correctly the position of the stimulated spot. Whenever localization was disturbed, the power of recognizing two compass-points applied consecutively was also affected.

Thermal sensibility was frequently intact in this group of cases. The impulses underlying heat and cold seem to run together in a distinct path, which not uncommonly escapes when the sensory loss is of the type at present under consideration. But if thermal sensibility is disturbed, heat and cold are affected together, after passing the thalamic junction.

Vibration of a tuning-fork could always be appreciated, but in the majority of cases in this group its duration appeared to be shortened; if the vibration of the fork seemed to have ceased on the affected half of the body, it could still be appreciated for from five to twenty seconds longer on a similar normal part.

Thus it would seem that sensory impulses travel from the optic thalamus to the cortex in five groups.

(1) Those concerned with the recognition of posture and passive movement. If these impulses are affected the power of discriminating weights on the unsupported hand may also be diminished.

(2) Certain tactile elements; integrity of this group is necessary for the discrimination of weights placed on the fully supported hand.

(3) Those impulses which underlie the appreciation of two points applied simultaneously (the compass-test); on this group also depends the recognition of size and shape.

(4) Those which underlie the power of localizing the situation of a stimulated spot. Recognition of the double nature of two points applied consecutively also depends on this group of impulses.

(5) All thermal impulses are grouped together to underlie a scale of sensations with heat at the one end and cold at the other. At the level with which we are now dealing these impulses have already excited the affective centre and are passing away to the cortex.

CHAPTER V.—THEORETICAL CONCLUSIONS.

So far we have described in detail the effects which may follow lesions situated in different parts of the brain. In the present chapter we shall attempt, by analysis of these results, to present a coherent account of the mechanism of sensation.

We believe there are two masses of grey matter, or sensory centres, in which afferent impulses end to evoke that psychical state called a sensation. One of these is situated in the optic thalamus, whilst the other consists of a considerable area of the cerebral cortex.

The anatomical structure known as the optic thalamus is an extremely complex portion of the brain, and contains not only the terminal centre for certain aspects of sensation, but plays a threefold part in the fate of sensory impulses:—

(1) Firstly, it contains the termination of all secondary paths; here sensory impulses are grouped afresh and redistributed in two directions, on the one hand to the cortex cerebri, and on the other to the grey matter of the optic thalamus itself (*vide* Chapter IV).

(2) Secondly, it contains a mass of grey matter, the essential organ of the thalamus, which forms the centre for certain fundamental elements of sensation. It is complementary to the sensory cortex and exercises different functions in the production of sensation.

(3) Lastly, the lateral part of the optic thalamus is the organ through which the cortex can influence the essential thalamic centre, controlling and checking its activity. The excessive response to affective stimuli, so prominent a feature of lesions in this situation, is not due to irritation but to removal of cortical control.

Next, we shall consider the nature of the activity of the sensory cortex. We shall show that it is concerned more particularly with discrimination and with the relation between two sensations, or between a sensation and its representation. It is essentially the organ by which attention can be concentrated on any part of the body.

Finally, we shall deal with the interaction of the cerebral cortex and the centre in the optic thalamus during the production of sensation.

§ 1.—*The Essential Activity of the Thalamic Centre.*

The most remarkable feature in that group of thalamic cases with which we have dealt in this work is not loss of sensation, but an excessive response to affective stimuli. This positive effect, an actual overloading of sensation with feeling tone, was present in all our

twenty-four cases of this class; and, though emphasis has not been laid upon it as a characteristic feature, it has been observed by others in cases where the existence of a lesion in the lateral zone of the optic thalamus was confirmed by autopsy (Roussy [35, 36], Edinger [8]).

This excessive response may be accompanied by much or by little loss of sensation, but the extent of this loss bears no relation to the amount of the over-reaction to painful stimuli. It is only necessary that sufficient sensory impulses, capable of exciting discomfort, should still be able to reach consciousness. If this is possible, the affected half of the body will respond more profoundly than normal parts to all painful stimuli, in spite of the gross loss of sensation. (Cf. Case 10, p. 222.)

But the characteristic thalamic response does not consist in an excessive reaction to painful stimuli only. In suitable cases we have shown that the response to pleasurable stimuli, such as warmth, is also greater on the affected side. Moreover, the manifestations of general mental states of pleasure and of discomfort may be more pronounced on the abnormal half of the body.

The pains and uncomfortable paræsthesiæ which occur in these cases have been explained by some observers as due to irritation. The lesion is supposed to irritate some part of the sensory path in the region of the optic thalamus and thus to produce pains and "hyperalgesia." But this conventional hypothesis is insufficient to explain the observed facts in the clinical course of these cases. In the large majority of instances the lesion has proved to be a hæmorrhage or a softening. Now all vascular lesions of the nervous system notoriously tend to produce the greatest disturbance of function at the time when they occur; the subsequent progress of the case always shows a certain amount of recovery. But in this group of thalamic cases the pains and over-reaction come on, as a rule, during the stage of recovery of function, frequently at a considerable period after the "stroke" has occurred, and they usually last unaltered for years.

Moreover, we have pointed out that the response to pleasurable stimuli is also increased in some of these cases, a condition incompatible with the constant existence of an irritative lesion which evokes pain.

Further, we have not found this peculiar over-response from lesions of other parts of the sensory path,¹ and the extreme rarity of such cases

¹ Spontaneous pains associated with over-sensitiveness to prick or other stimuli have been described as a consequence of lesions of the central nervous system at other parts of the sensory path, but few of these cases will stand criticism. For example, in the case published by Raymond and Rose [32] as a lesion of the pons varolii the authors themselves admit the possibility of multiple lesions, and the presence of choreic and athetoid movements points in all

in the literature compared with the overwhelming frequency of this over-response with the lesions of the optic thalamus, compels us to adopt some other explanation for its occurrence at this level of the nervous system.

It is obvious, therefore, that the attempt to explain this condition by a hypothetical irritation fails entirely, and we must consider whether the clue is not to be discovered in the removal of some control normally exerted by one sensory centre upon another.¹

Let us turn for a moment to the motor side of the nervous system, where the effects produced by removal of control are more fully understood. It is well known that a lesion of the motor region of the cerebral cortex, or of the tracts which run from it to the spinal cord, produces not only loss of voluntary movement, but also a positive effect in the increased tone and rigidity of the affected limbs. This increase of tone, as Hughlings Jackson [15] pointed out in the Croonian Lectures nearly thirty years ago, is not the direct effect of the destructive lesion, but is produced by the activity of subcortical centres released from control. He laid down the law that no destructive lesion can produce a positive effect directly. The activity of the cortex cerebri normally inhibits and controls subcortical motor centres and the destructive lesion sets these centres free to display their powers unchecked. Loss of voluntary power is consequently associated with tonic over-action and an increased reflex discharge in response to afferent impulses.

We believe that an exactly similar condition is revealed on the sensory side of the nervous system by cases of thalamic disease accompanied by an excessive response to peripheral stimuli. We know that paths run, not only from the optic thalamus to the cortex, but from the cortex to the thalamus, and they have been shown ([25] [4] [38]) to terminate in its lateral zone, the very region affected in cases that have exhibited the "syndrome thalamique." But, since these paths come from all parts of the cortex to impinge upon the optic thalamus the functions they exercise cannot be removed by partial destruction of the cerebral

probability to affection of the optic thalamus. Raymond and Français [31] recorded a pontine case in which pains and "hyperæsthesia" to prick were present, but the position of the lesion was not determined by autopsy. In Mann's case [22] there was merely persistent unilateral pain, and Mann himself recognized that this was accompanied by "hypæsthesia" and not by "hyperæsthesia," as in Edinger's case of thalamic disease, with which he contrasted it.

¹ The condition known as protopathic sensibility, arising from lesions of peripheral nerves, is also characterized by an over-response to painful and to thermal cutaneous stimuli. This over-response is due to the uncontrolled action, on normal sensory centres, of impulses capable of exciting sensations heavily charged with feeling-tone (Rivers and Head [33]). But full discussion of the relation between protopathic sensibility and the condition produced by thalamic lesions must be reserved for a subsequent communication.

hemispheres; cortical lesions produce no thalamic over-response to affective stimuli. The only certain method of releasing the optic thalamus from the influence exerted by the cortex is to destroy the lateral nucleus in which the majority of these cortico-thalamic paths seem to end. It is probable that a subcortical lesion so situated that it destroyed all these paths just before they entered the thalamus might produce the "syndrome thalamique," although the substance of this organ remained intact; but such lesions must be rare compared with those which produce this effect by destruction of part of the thalamus itself.

The only function which can be ascribed to these cortico-thalamic paths is that through them the cortex controls, in some way, the activity of the thalamus. If this view is correct, lesions which interrupt these paths, but leave intact the main substance of the optic thalamus, must lead to a permanent over-activity of functions exercised by that organ. Any afferent impulses, which are capable of exciting this part of the brain, will act on an uncontrolled centre and must, consequently, evoke an excessive effect.

All stimuli which produce an excessive effect, when the thalamus is freed from cortical control, contain elements which can excite the essential centre of this organ. Analysis of the over-response in these thalamic cases will, therefore, reveal what sensory qualities are due to the activity of the optic thalamus. Now we have shown that the nearer a sensation approaches pure discomfort, the more certainly will the response be exaggerated on the affected half of the body. States of pleasure and stimuli, such as warmth, capable of exciting pleasurable sensations, may also evoke excessive manifestations on the abnormal side. Since, therefore, affective states can be increased when the thalamus is freed from cortical control, we may conclude that the activity of the essential thalamic centre is mainly occupied with the affective side of sensation.

This conclusion is strengthened by the fact that stationary cortical lesions, however extensive, which cause no convulsions or other signs of irritation and shock, produce no effect on sensibility to pain. Destruction of the cortex alone does not disturb the threshold for the painful or uncomfortable aspects of sensation.

Some stimuli, not usually included amongst those which evoke pleasure and discomfort, may produce an exaggerated response when the grey matter of the optic thalamus is free to react unimpeded. Thus, cotton-wool moving over a hair-clad part may produce a "stronger" sensation on the abnormal half of the body. Roughness is another stimulus

which appeals to the essential thalamic centre and not uncommonly produces an exaggerated response over affected parts. The vibration of a tuning-fork, applied to the surface of the body, also contains an element which may produce an excessive effect and, in most cases, although the length of time during which the vibrations are appreciated is materially shortened, the patient asserts that the sensation is "stronger" on the abnormal side.

But all these stimuli evoke sensations more or less allied to tickling and scraping, and it is not surprising that the affective element should be exaggerated. We believe, however, that an appeal can be made to the essential thalamic centre by stimuli which produce changes of internal state other than those of pleasure and discomfort. A cortical lesion never abolishes sensibility to contact; the response may be intermittent, irregular, and grossly defective, but is never completely absent. A weight resting on the hand may not be recognized, but at the moment it is placed on the skin and, not infrequently, when it is removed, or even gently touched, the patient says that "something has happened." When the loss of sensation is extremely severe, and all sensory impulses passing to the cortex have been cut off, the patient may be unable to recognize that the effect he experiences is produced by an external object and may simply reply that something is happening to him. These contact-stimuli, which may produce this vague sensation of "something happening" within the body, evoke precise recognition that an object is acting on its surface when the cortical paths are intact. Under normal circumstances the thalamic element in contact-sensibility rarely, if ever, reaches consciousness, which is dominated by discriminative sensations of touch, and it only becomes a conscious factor in sensation when the influence of the cortex is removed.

Thus, we believe that the essential organ of the optic thalamus is the centre of consciousness for certain elements of sensation. It responds to all stimuli capable of evoking either pleasure and discomfort, or consciousness of a change in state. The feeling-tone of somatic or visceral sensation is the product of thalamic activity, and the fact that a sensation is devoid of feeling-tone shows that the impulses which underlie its production make no thalamic appeal.

The functions of this organ are influenced by the coincident activity of the cortical centres, and this control is effected by means of paths from the cortex to the thalamus which probably end in its lateral nucleus. Injury in this region sets free the thalamic centre from control and it can therefore react without restraint to all stimuli capable of

arousing affective states. Since, however, most stimuli which act upon the body in daily life are noxious and so contain a disagreeable element, most sensations experienced by the patient with a lesion of the optic thalamus are painful. This is particularly the case when sensation is so gravely diminished that stimuli of great intensity only can reach consciousness. The occurrence of spontaneous pains and the painful paræsthesiæ of the affected half of the body, so constant a feature of these cases, are due to the uncontrolled activity of this centre through which painful stimuli evoke a disagreeable sensation.

§ 2.—*The Nature of the Sensory Activity of the Cortex.*

In a previous chapter we have described the results produced by a cortical lesion upon a series of measured sensory tests. Let us now analyse these defects in the hope that thereby we may learn the part played by the cortex in that response to an external stimulus we call a sensation.

We are not concerned here with the limits of the area on the surface of the brain which are associated with a disturbance of sensibility; before it is possible to talk of "cortical localization" we must know what sensory qualities are due to the activity of the cortex. Much of the doubt that still hangs round the topography of "sensory centres" arises from this ignorance. Most observers start with the assumption that impulses originate in peripheral end-organs and pass unaltered to the cortex, there to underlie that psychical state we call a sensation. But we have already seen that the impulses upon which depend the "primary sensations" of touch, pain, heat and cold, are highly complex and undergo much regrouping before they arrive at the final sensory centres.

Afferent impulses on their way from the periphery to the cortex pay toll first of all to the unconscious co-ordinating mechanisms of the spinal cord and the cerebellum. Then, after being regrouped at the thalamic junction, they act upon two terminal centres. One of these, the essential organ of the optic thalamus, responds to all those elements which can evoke consciousness of an internal change in state, more particularly pleasure and discomfort. Sensory impulses then pass by way of the internal capsule to act upon the cortex and these are the afferent materials out of which the cortex manufactures the forms of sensation with which it is concerned.

We know the nature of these impulses as they travel through the capsule to the cortex; it is revealed by those cases of thalamic and

capsular disease in which the loss of sensation is due to interference with paths which pass from the optic thalamus to the sensory cortex (*vide* p. 174).

The dissociations of sensibility which can occur under such conditions show that, after exciting the essential centre of the optic thalamus, sensory impulses pass on in five main groups to be distributed to the cortex :—

(1) Those which underlie postural recognition and the appreciation of passive movement. Upon this group depends the secondary faculty of judging the difference or identity of two weights placed on the unsupported hands.

(2) Impulses which underlie the recognition of tactile differences or the power of appreciating those qualities of touch other than contact and roughness. To this group we owe the faculty of recognizing the increase or diminution in weight of a test-object, and of distinguishing the difference between two weights placed on the supported hand.

(3) Those upon which depend spacial discrimination (compass-points applied simultaneously) and its allied faculty, the recognition of size and shape.

(4) Those impulses which enable the patient to recognize the spot stimulated (localization). They carry with them the power of appreciating the double nature of two points applied to the surface one after the other.

(5) Thermal impulses. On this group depends the possibility of recognizing those degrees of temperature which necessitate a comparison with the consequences of some previous thermal sensation.

Such are the afferent materials out of which the cortex manufactures those forms of sensation for which it is responsible. We have already studied the nature of this activity, as revealed by the effects of a cortical lesion (Chapter III). Such a lesion tends, as we have seen, to produce peculiarities in the response to sensory stimuli unknown at any other level of the nervous system. The larger the area affected between the precentral fissure and the occipital lobe, the more certainly will sensibility show these characteristic changes.

The accuracy of response to measured tactile stimuli, whether von Frey's hairs or graduated pressure, is greatly reduced. The answers are irregular and uncertain, and increasing the stimulus does not of necessity lead to an equivalent improvement in the proportion of accurate replies. Contact-sensibility is not lost, and cotton-wool may still be appreciated, although it may seem "less plain" than on the normal

side. Tactile sensations tend to persist and hallucinations may be present to an abnormal degree. Fatigue is induced with unusual facility; this is not general but affects solely the sensibility of the affected part, for the answers from the normal side may remain as good at the end as at the beginning of a series of observations.

The power of estimating the relative warmth or coldness of two stimuli suffers when thermal sensibility is affected by a cortical lesion. That part of the scale can no longer be appreciated where the sensation evoked by a given temperature normally depends on that to which the part has been previously adapted. This zone of relative heat and cold is abolished over the affected parts, and temperatures that fall within it are said to be neutral. Even when the warmth or coldness of the stimulus can be correctly appreciated, the sensation seems "less plain" over the affected limbs; the replies of the patient are less constant and less certain, and a temperature recognized without difficulty at one time seems doubtful at another. The power of discriminating the relative coolness of two cold stimuli and the relative warmth of two hot tubes is diminished, provided two temperatures are chosen which do not appeal differently to the thalamic sensory centre. Thus even the faculty of appreciating the relative intensity of two temperatures on the same side of the scale is disturbed, although both may be named correctly.

But all these stimuli contain elements capable of rousing the activity of the essential thalamic centre. The tests for the recognition of posture, of passive movement, spacial discrimination (compasses) and the locality of the stimulated spot contain no such elements, and it is these aspects of sensation that suffer most profoundly in consequence of a lesion of the sensory cortex. Postural recognition and the appreciation of passive movements are usually grossly affected. The power of localizing the stimulated spot is less frequently disturbed, but may be abolished. These two faculties are independent of one another and may be affected separately. Moreover, a disturbance of localization caused by a lesion of the cortex is not due to coincident uncertainty of tactile sensibility, for it is equally demonstrable when the stimulus is a prick to which the patient responds on every occasion.

A cortical lesion can destroy the power of appreciating the double nature of the compass-points applied simultaneously to the skin; increasing the distance between them may not, under such circumstances, improve the accuracy of the replies. This loss is in no way due to defects of tactile sensibility, for it can be demonstrated when the compasses are armed with two sharp points.

When dealing with the arrangement of the sensory impulses which pass through the internal capsule to be distributed to the cortex, we showed that the power of estimating weight, size, shape and form in three dimensions depends on the integrity of several separate groups. Thus the appreciation of difference between two weights placed in the unsupported hand demands perfect postural recognition. The faculty of estimating weights placed consecutively on the supported hand depends on the integrity of tactile sensibility. Such dissociation is impossible with lesions of the cortex, for we are no longer dealing with a disturbance of sensory impulses, but with the difficulty of recognizing the relation between two percepts. The patient generally gives up all attempts at appreciation, saying he has "no idea" of the shape, form, or relative size and weight of the test-object.

The tests for the appreciation of roughness and of texture demonstrate clearly the part played by the cortex in sensation. With Graham-Brown's æsthesiometer the threshold is identical on both hands; in every case the amount of protrusion necessary to make the flat surface of the instrument seem rough is the same on the two sides. In this test the patient has to determine solely whether the sensation is one of roughness or smoothness. But, as soon as he is asked to correlate these sensations and combine them with those of touch, as in the tests for the appreciation of texture, he fails entirely. He complains that from the affected hand he can gain no idea of the relation between the various stuffs passing under his fingers. One may seem rough, another smooth, but the sensations do not enable him to recognize the material he is handling.

Evidently, one of the faculties which we owe to cortical activity is the power of relating one sensation to another, whether they arise simultaneously or consecutively. Recognition of weight, size, shape, form and texture depends entirely on this faculty. Such tests consequently reveal the grossest defects whenever a cortical lesion produces any considerable influence upon sensibility.

A little consideration shows that loss of this faculty of relation is at the bottom of the diminished appreciation of posture and passive movement, which constantly forms one of the gravest defects produced by lesions of the cortex. For it would be impossible to discover the position of any part of the body, unless the immediate postural sensations were related to something that had preceded them. A direct perception of posture, analogous to that of roughness, is impossible; in every case the new position of the limb is relative to some previous posture.

At any moment we can become conscious of the position of any part of our bodies, and although such postural recognition is not constantly in the central field of attention, it always forms the measure against which we judge subsequent change. This is peculiarly the case with the appreciation of passive movement. Not uncommonly a patient with a cortical lesion can recognize that some movement has occurred, but is entirely unable to discover its direction or amplitude; complete appreciation of passive movement is the recognition of serial changes in a certain direction.

Munk [27] and all those who have recognized the relative nature of the appreciation of posture and passive movement have spoken of the cortex as the repository of images of movement. This is, however, an unsatisfactory term when we consider the actual effects produced by a cortical lesion; for, when we speak of a visual or of an auditory image, we mean something that can be recalled into consciousness. If we compare the colour of one ribbon with that of another seen a few moments before, many of us can recall the image of the first and compare it with that of the second. Both may be in the central field of consciousness together.

When we sit immobile and imagine our fingers touching some object on the table, many of us see, at once, the picture of an outstretched arm; the only image in consciousness is a visual one. Now, in cases where all power of recognizing posture is lost this visual image remains unchanged, and it cannot therefore be the standard to which we refer alterations in posture. Place the patient's affected arm in front of him on the bed, allowing him to see the position in which it lies; close his eyes, and in most cases he will see a mental picture of his hand. Then change its position whilst his eyes remain closed and he will continue to see a picture of the hand in its old position. Moreover, if localization is not affected, he will name correctly the spot stimulated but will refer it to the position in which he visualizes the hand. The visual image of the limb remains intact, although the power of appreciating changes in position is abolished.

It is evident, therefore, that the standard resulting from previous postures and movements, to which immediate reference is made when a fresh position is recognized, cannot be a visual image. The existence of a group of human beings whose conscious life by day is devoid of all visual images would be sufficient evidence of this fact apart even from the direct results of experiment. Some such persons may possess true movement images. That is to say, the

assumption of an imagined posture may be accompanied by re-presentations of movement equivalent to the pictures of those who visualize strongly.

But in both cases the image, whether it be visual or motor, is not the fundamental standard against which all postural changes are measured. Every recognizable change enters into consciousness already charged with its relation to something that has gone before, just as on a taximeter the distance is presented to us already transformed into shillings and pence. So the final product of the tests for the appreciation of posture or passive movement rises into consciousness as a measured postural change.

For this combined standard, against which all subsequent changes of posture are measured before they enter consciousness, we propose the word "schema." By means of perpetual alterations in position we are always building up a postural model of ourselves which constantly changes. Every new posture or movement is recorded on this plastic schema, and the activity of the cortex brings every fresh group of sensations evoked by altered posture into relation with it. Immediate postural recognition follows as soon as the relation is complete.

One of our patients had lost his left leg some time before the appearance of the cerebral lesion which destroyed the power of recognizing posture. After the amputation, as in so many similar cases, he experienced movements in a phantom foot and leg. But these ceased immediately on the occurrence of the cerebral lesion; the stroke which abolished all recognition of posture destroyed at the same time the phantom limb.

In the same way, recognition of the locality of the stimulated spot demands the reference to another "schema." For a patient may be able to name correctly, and indicate on a diagram or on another person's hand, the exact position of the spot touched or pricked, and yet be ignorant of the position in space of the limb upon which it lies. This is well shown in Hn. (Case 14), who never failed to localize the stimulated spot correctly, although he could not tell the position of his hand. This faculty of localization is evidently associated with the existence of another schema or model of the surface of our bodies which also can be destroyed by a cortical lesion. The patient then complains that he has no idea where he has been touched. He knows that a contact has occurred, but he cannot tell where it has taken place on the surface of the affected part.

It is to the existence of these "schemata" that we owe the power of projecting our recognition of posture, movement and locality beyond the limits of our own bodies to the end of some instrument held in the hand. Without them we could not probe with a stick, nor use a spoon unless our eyes were fixed upon the plate. Anything which participates in the conscious movement of our bodies is added to the model of ourselves and becomes part of these schemata: a woman's power of localization may extend to the feather in her hat.

Thus, it is evident that among the various functions of cortical activity which imply a relation, the act of comparison may be of different grades in the hierarchy of consciousness. The appreciation of two weights placed at the same time one in each hand is an example of the faculty of relating two groups of presentations simultaneously in the focus of consciousness.

Recognition of posture and passive movement implies the combination of every fresh group of sensations with postural schemata outside the central field of attention. The change in consciousness which corresponds to this combination is immediate recognition of an altered position.

But such disturbance of the power of recognizing identity and difference will not account for all the abnormalities of sensation produced by a cortical lesion. When the affected part is under examination, the patient's replies are uncertain and variable; hallucinations and persistence of sensation tend to disturb the records. They show in an exaggerated form the errors that may appear in a normal person who is inattentive. And yet, as soon as we examine any unaffected part, the patient may come through the same series of tests without a mistake. On the left hand in Case 14, the records were on one occasion so bad that we took a similar series of readings, not only from the other hand, but also from both feet; those from the affected hand alone showed the features which might have been attributed to inattention.

Moreover, in many cases increasing the strength of the tactile stimulus does not of necessity produce a corresponding improvement in the answers. As good a record may be obtained with a hair exerting a pressure of 0.36 grm. as with one of ten times the strength. In the same way as many correct answers may be given to the contact of an instrument weighing 2 grm. as when it exerts a pressure of 32 grm. on the same area.

Evidently a lesion of the cortex produces an effect upon sensation of a different order from that found at any lower level of the nervous

system. All those defects, which may occur when a normal person is under examination with psychophysical tests, are present in a grossly exaggerated form. Those defects, which we ordinarily attribute to want of attention, are raised to a degree unknown in the normal human being. But the patient's power of general attention has not been lowered in such cases as those we have cited in this paper. Records from the limbs of the sound side show that the phenomena of defective attention are confined to the abnormal parts. A portion only of the patient has, as it were, become untrustworthy.

We believe that the functional integrity of the cortex enables attention to be concentrated upon those changes which are produced by the arrival of afferent impulses. When this is disturbed, some impulses evoke a sensation, but others, from lack of attention, do not affect consciousness. Attention no longer moves freely over the sensory field to be focussed successively on fresh groups of sensory impressions. Sensations, once evoked, are not cut short by the moving away of the focus of attention as when cortical activity is perfect. Hence arise persistent sensations and hallucinations which are so prominent a feature after lesions of the cortex.

To sum up, we believe that the cerebral cortex is the organ by which we are able to focus attention upon the changes evoked by sensory impulses. A pure cortical lesion, which is not advancing or causing periodic discharges, will change the sensibility of the affected parts in such a way that the patient's answers appear to be untrustworthy. Such diminished power of attention makes the estimation of a threshold in many cases impossible. Uncertainty of response destroys all power of comparing one set of impressions with another and so prevents discrimination.

But, in addition to its function as an organ of local attention, the sensory cortex is also the storehouse of past impressions. These may rise into consciousness as images, but more often, as in the case of spacial impressions, remain outside central consciousness. Here they form organized models of ourselves which may be termed "schemata." Such schemata modify the impressions produced by incoming sensory impulses in such a way that the final sensations of position, or of locality, rise into consciousness charged with a relation to something that has happened before. Destruction of such "schemata" by a lesion of the cortex renders impossible all recognition of posture or of the locality of a stimulated spot in the affected part of the body.

§ 3.—*The Inter-relation of the Optic Thalamus and the Cortex in the Production of Sensation.*

In daily life all stimuli excite more or less both thalamic and cortical centres, for most unselected sensations contain both affective and discriminative elements. But, amongst the tests we have employed in sensory analysis, some appeal almost entirely to the one or other centre. The test for recognition of posture, as carried out by us, is purely discriminative; whilst the pain produced by squeezing the testicle, or to a less degree by the pressure-algometer, appeals almost exclusively to the more affective centre.

Sensory impulses arriving at the optic thalamus are regrouped in such a way that they can act upon both its essential centre and the sensory cortex. The essential organ of the thalamus is excited to affective activity by certain impulses, and refuses to react to those which underlie the purely discriminative aspects of sensation. These pass on to influence the cortical centres where they are readily accepted. In a similar way, the primary centres of the cortex cannot receive those components which underlie feeling-tone; in this direction they are completely blocked.

It has long been recognized that sensations are endowed with feeling-tone to different degrees. In those which underlie postural appreciation this quality is entirely absent, whilst visceral sensations are, in some instances, little more than a change in a general feeling-tone; one set of impulses appeals almost exclusively to the cortical centre, the other to that of the optic thalamus. All thermal stimuli, however, make a double appeal. Every sensation of heat or cold is either comfortable or uncomfortable; the only entirely indifferent temperature is one that is neither hot nor cold.

In the same way, most unselected tactile stimuli appeal both to the sensory cortex and to the optic thalamus. For not only is a touch always related to, and distinguished from, something that has gone before it, but we have shown that contact, especially of an object moving over hair-clad parts, is capable of exciting thalamic activity. Vibrations of the tuning-fork also make a double appeal, for when the cortical paths are cut the amplitude of the vibration must be greater in order that it may be appreciated; on the other hand, the vibratory effect may be stronger on the abnormal side in those thalamic cases where the affective response is excessive.

But these two centres of consciousness are not co-equal and

independent. Under normal conditions the activity of the thalamic centre, though of a different nature, is dominated by that of the cortex. When we examine the sensation normally produced by a prick, we recognize that the pain develops slowly and lasts a considerable time after the stimulus has ceased. Moreover, the same intensity of stimulation will produce a different effect on the same spot on different occasions. A long, latent period, persistence, and want of uniformity are characteristic of all painful sensations. This is seen in an exaggerated form in cases where the thalamic centre has been freed from control. The response to prick is slow, but persists long after the stimulus has ceased. Moreover, the reaction, when it occurs, tends to be explosive; it is as if a spark had fired a magazine and the consequences were not commensurate with the cause.

On the contrary, the sensations normally produced by moderate tactile stimuli are characterized by a short latent period, and disappear almost immediately on the cessation of the stimulus. A lesion of the sensory cortex disturbs both these characteristics. Tactile sensations became uncertain and incalculable, and no threshold can be obtained; persistence and hallucinations mar the uniformity of the records.

Now we have shown that the sensory cortex is the organ by which attention can be concentrated on any part of the body that is stimulated. The focus of attention is arrested by the changes produced by cortical activity at any one spot. These are sorted out and brought into relation with other sensory processes, past or present. Then the focus of attention sweeps on, attracted by some other object.

All stimuli which appeal to the thalamic centre have a high threshold. They must reach a high intensity before they can enter consciousness, but once they have risen above the threshold they tend to produce a change of excessive amount and duration, and this it is the business of the cortical mechanism to control. The low intensity of the stimuli that can arouse the sensory cortex, and its quick reaction-period, enable it to control the activity of the cumbersome mechanism of the thalamic centre.

Our view of the sensory mechanism put forward in this paper explains many of the facts already recognized both by psychologists and clinicians. It enables us to understand how integration can occur at all afferent levels of the nervous system, and makes development possible even in the individual. The aim of human evolution is the domination of feeling and instinct by discriminative mental activities. This

struggle on the highest plane of mental life is begun at the lowest afferent level, and the issue becomes more clearly defined the nearer sensory impulses approach the field of consciousness.

APPENDIX I.

METHODS USED FOR EXAMINING SENSATION.

THE value of our work depends entirely on the trustworthiness of the methods used in our investigations, and we shall therefore devote this appendix to a short consideration of the means we have adopted to test sensation. This is the more necessary because they stand midway between the rough-and-ready tests of the clinician and the elaborate methods of the psychophysical investigator. Extended observations with cumbersome apparatus are possible to the latter, because he is working with normal human beings, who can be selected and trained for his purpose.

Our aim has been to employ a series of tests which give measurable results without, at the same time, exhausting the patient, or demanding any but the smallest amount of introspection. The measurements so obtained are not compared with an absolute standard, but with the results yielded by the same tests on the normal half of the patient under identical conditions, and we have therefore rejected all cases where both sides were affected.

Even on the normal side we do not attempt, in most instances, to discover the true threshold. We begin each series of observations on the normal half of the body with a test near the threshold-value, but well within the patient's capacity. The abnormal parts are then examined with the same test, and, if a perfect series of answers cannot be obtained, the stimulus is increased until a threshold is reached, or, if this is not possible, until the task is at least many times easier than is necessary on the normal side. Thus, all our measurements are comparative, and each case yields its own standard. Otherwise such tests as the compasses, recognition of relative weight and size, and all attempts to estimate painful stimuli are useless and fallacious for observations on the sick.

Measurable stimuli are also necessary when we wish to compare

the reaction evoked from normal and affected parts. For instance, it is impossible to study satisfactorily the results produced by a prick over so-called "hyperalgesic" areas, unless we can be certain that the force behind the needle is approximately the same with every stimulation.

We have always attempted to analyse composite forms of sensation into their simplest components. For instance, the power of recognizing the form of an object by handling it depends on the integrity of several simple sensory qualities, and the condition of each of these components must be investigated if the exact nature of the more complex loss is to be understood. Similarly, the faculty described as "topognosis," the power of pointing without the aid of vision to the stimulated spot, may be affected either by loss of the sense of locality, or by ignorance of the position in space of the part of the body upon which that spot is situated; on which of these the atognosis depends can be determined only when the two faculties are separately examined. On the other hand, the condition of the more complex faculties must be tested in each case, since they depend on the power of associating in consciousness several different elementary qualities of sensation.

But it is also necessary that the tests employed should be suitable for ordinary clinical purposes. Although several of our most interesting cases have been drawn from private practice, the majority of our patients belonged to the hospital class, who are, as a rule, poorly educated and not highly intelligent, and in examining them it is obviously impossible to make use of the more elaborate tests that are employed by psychologists. The difficulty in attempting this is increased by the fact that the lesions which produce the symptoms we have investigated, or associated pathological changes, frequently lower the intellectual activity of the subjects. An attempt to employ such tests in unsuitable cases not only leads to an undue expenditure of time, but may readily give rise to error and confusion.

Early in our studies we drew up a schedule or scheme, according to which all forms of sensibility could be systematically investigated. This has been in many respects modified or elaborated in the course of our work, and is presented here in the form in which we now employ it (p. 211).

Such an examination as this schedule demands needs much time and patience on the part of both the observer and the patient, even when it is carried out on a small portion of the body. Each of our cases required, as a rule, five to ten hours divided into several sittings, and

in many instances we devoted a much longer time to the examination. These facts may seem to make our methods unsuitable for ordinary clinical purposes, but our aim has been to investigate completely the nature of the changes in sensation rather than to discover signs of diagnostic utility. For this purpose a much shorter and simpler scheme may be drawn up.

Those who wish to repeat our observations must either employ the methods we have followed or must select others more accurately suited to the purpose. It is useless to attempt either to confirm or controvert our results by tests carried out on the usual lines of clinical examination.

Certain well-recognized rules have always guided our studies. The most important of these is to obtain the goodwill and interest of the patient; for without this it cannot be hoped that the observations will be trustworthy. When attention begins to flag, or the patient to tire or lose interest, it is necessary to interrupt the examination; and for this reason we have always tried to arrange that the tests demanding the greatest effort and concentration on the part of the patient should be made early in the sitting while he is fresh, and the coarser and subjectively easier tests reserved till the later stages.

In the second place, we have always avoided, as far as possible, anything that might, on the one hand, suggest a response, or, on the other, confuse it. Each test was first explained fully to the patient, and he was requested to reply simply "yes" or "no," or by other appropriate answer to each stimulus. No further questions were asked during the examination. In many instances it is necessary to obtain, in addition, an introspective description or analysis of the sensation evoked; but we have always attempted to separate this from the tests that were devoted to the determination of any alteration of sensibility.

(A) SPONTANEOUS SENSATIONS.

The examination is begun by obtaining from the patient a description of any abnormal sensations he may experience in the affected parts, such as pain, numbness or tingling. As these terms may imply very different conditions in ordinary phraseology, it is necessary to determine as exactly as possible in what sense they are used by the patient. "Numbness" may signify a "loss of feeling," or it may even be used to describe, not a loss of function, but a positive abnormal sensation, a *paræsthesia*.

When such spontaneous sensations exist, it is important to ascertain if they are constant, or the conditions under which they occur, and if they are aggravated by any external agent, as contact, heat or cold.

We are accustomed to inquire also if the patient has noticed at any time that he is unaware of the position in which the affected limbs lie, and if he preserves an idea or mental picture of the limb. Many patients complain that when they wake at night they do not know where the arm is lying, and in some cases it seems as if part of the limb, such as the hand, had disappeared.

(B) LOSS OF SENSATION.

(1) *Touch.*

Whilst investigating the state of tactile sensibility, the part to be tested is always screened from the patient's sight and he is asked to reply "yes" to each contact he appreciates. In no case is he questioned during the progress of the observations.

At first we were in the habit of blindfolding our patients, but, especially in cases of cerebral disease, this is liable to lead to a state of defective general attention. These patients usually prefer to keep their eyes open and we arrange the screen so that not only the part to be tested but also the manipulations of the observer are hidden from sight.

(a) *Light touch* is always examined first by applying a wisp of fine cotton-wool of long fibre gently to the skin so that it does not produce gross pressure or any deformation of structure. By this test any considerable loss of sensation can be easily detected on hairless parts; but cotton-wool contacts are frequently appreciated over hair-clad regions which are insensitive to this stimulus when the hair has been removed by shaving. In the same way the palm, the palmar aspect of the fingers and the dorsal surface of the terminal phalanges, which are devoid of hairs, are often insensitive to cotton-wool, though such contacts may be appreciated on the hair-clad portions of the hand. This is in part due to the fact that a stimulus which bends a hair is magnified by leverage in its effect on the afferent end-organs. But in the class of case with which we deal in this research a more important factor is the "tickling" produced over hair-clad parts by contact with cotton-wool. Owing to this affective element in hair-sensibility, hair-clad parts may remain sensitive to contact with cotton-wool even though sensation to this stimulus is lost over hairless parts.

For determining the threshold for light touch, we have employed

von Frey's graduated hairs, which depend upon the fact that a constant pressure is exerted on the tip of a hair when sufficient force is used to bend it. Now it is obvious that we can arrive at the pressure per unit area if the force exerted in bending the hair, measured on a balance, is divided by its total area in mm.^2 ; the result is expressed in gm./mm.^2 . The numbers by which von Frey's hairs are known throughout this paper depend on this method of calculating their effect.

But von Frey states [9] that this is not a correct method of comparing hairs which are used as graduated tactile stimuli. For this purpose he divides the pressure in milligrammes by the radius of a circle of the same area as the cross-section of the hair. The result expressed in gm./mm. represents the tension of the hair.

In the following table we give the actual pressure exerted by each hair, the measurements of its surface, the pressure exerted per unit area, and the tension.

Number by which the hair is known	Pressure in grammes	Measured radii μ	Total area in mm.^2	Radius of a circle of the same area in μ	Pressure per unit area	Tension
8	0.04	30 x 54	0.005	40	8 gm./mm.^2	1 gm./mm.
12	0.1	47.5 x 57.5	0.0085	52	12 gm./mm.^2	2 gm./mm.
14	0.21	55 x 90	0.015	70	14 gm./mm.^2	3 gm./mm.
21	0.23	40 x 80	0.011	58	21 gm./mm.^2	4 gm./mm.
21	0.36	60 x 90	0.017	73.5	21 gm./mm.^2	5 gm./mm.
28	0.88	100 x 120	0.0377	110	28 gm./mm.^2	8 gm./mm.
35	1.4	100 x 130	0.041	114	35 gm./mm.^2	12 gm./mm.
40	1.8	115 x 125	0.045	120	40 gm./mm.^2	15 gm./mm.
70	3	115 x 115	0.042	115	70 gm./mm.^2	26 gm./mm.
90	3.6	100 x 130	0.041	114	90 gm./mm.^2	33 gm./mm.
100	3.5	80 x 140	0.035	110	100 gm./mm.^2	32 gm./mm.
110	4.8	105 x 130	0.044	120	110 gm./mm.^2	40 gm./mm.

Hairs exerting a pressure of more than 100 gm./mm.^2 may cause a sensation of pricking, especially over sensitive parts of the hand, and we have therefore avoided their use in all observations on tactile sensibility.

The hand and forearm are the most suitable site for the use of von Frey's hairs and in the majority of our patients the greater disturbance of function fell upon one upper extremity. By previous rough tests an area is selected, usually on some part of the hand, where we have reason to suspect that sensation is disturbed. Testing is begun on a similar part of the normal hand with a hair to which the patient can give a perfect series of answers without difficulty. Most parts of the hand in normal persons react to hairs of 8 to 12 gm./mm.^2 , and 21 gm./mm.^2 is therefore well above the normal threshold. Sixteen

contacts are made in one minute, a rate which allows us to vary the intervals between any two touches in order to avoid the common tendency to rhythmical replies, especially from areas of defective sensibility. On the abnormal side, the first hair selected is that which can be easily appreciated on the normal hand; then hair after hair of increasing strength is applied until either the threshold is passed

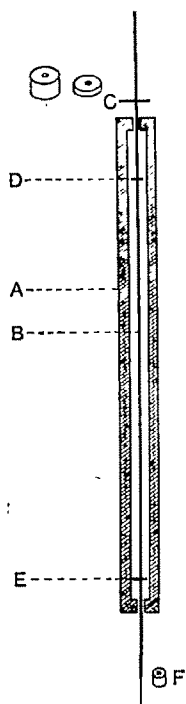


FIG. 5.—The pressure-aesthesiometer.

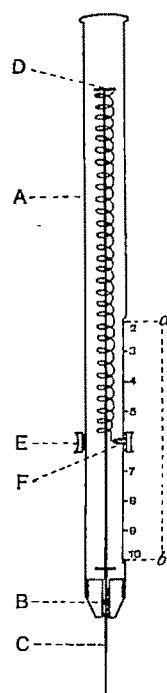


FIG. 6.—The spring-algesimeter.¹

or the strongest hair which does not produce pricking is reached. Frequently we then go backwards again to the hair with which the testing had begun. No word is spoken throughout such a series of tests, which always end in a final set of contacts on the normal hand of the same hair with which we had begun.

Each correct answer is recorded by a vertical stroke and failure to reply by an O; hallucinatory responses, if they occur, are marked with a broken stroke. From such a record the proportion of correct replies, and the order in which they occurred, can be studied at leisure. (For an example of these records see pp. 138, 148, 237.)

¹ This and other instruments, described for the first time in this paper, were made by Mr. C. F. Palmer, 6, Upper Tulse Hill, S.E.

(b) *Pressure-touch* can be roughly tested by contact with the pulp of the observer's finger, provided that its surface-temperature does not differ widely from that of the part to be examined.

For the determination of the threshold for pressure-touch we have employed a simple form of pressure-æsthesiometer (fig. 5). This consists of a vulcanite cylinder (A) pierced in its length to allow a thin steel rod (B) to move freely in it. Each end of this rod projects some distance beyond the ends of the cylinder; one end is pointed and shod with a cork or vulcanite disc 3 mm. in diameter (F), which we have adopted as a standard area, while near the other end there is a small platform (C) on which weights, pierced in their centre, so that they can be placed on the steel rod, may rest. The weight of the steel rod with the contact disc is 2 grm., and this is consequently the weight that falls on the skin through the disc when the unloaded instrument is brought vertically in contact with it; but by adding weights this pressure can be increased up to 50 grm. or more if necessary. The instrument is held by the vulcanite cylinder and the cork disc is brought gently in contact with the part to be tested; then by depressing the cylinder the desired weight falls on the surface. The instrument is simple and suffers only from the disadvantage that it must be used vertically. The minimal pressure that can be applied by it is necessarily high owing to the weight of the steel rod, but can be reduced to 1 grm. This pressure on a 3 mm. disc can be always and constantly appreciated on normal parts, and the instrument is consequently of use only after tests with von Frey's hairs or cotton-wool have shown that there is an alteration of tactile sensibility.

In attempting to determine a threshold with this æsthesiometer we adopt the procedure described for von Frey's hairs, beginning with a low pressure and increasing after each series of contacts until a weight is reached with which the sixteen successive contacts in one minute can be appreciated (cf. p. 150).

(2) *Localization.*

Various methods have been described to test the faculty of localization of tactile and other stimuli on the surface of the body. We have experimented with most of them, but have found a modification of Henri's method the most suitable for clinical purposes.

In Henri's original method the patient was required to mark on a life-sized diagram or photograph the exact situation of the spot

stimulated, while the observer indicated on a duplicate diagram the spot he touched. Simple though this method is, it labours under the disadvantage that many patients find a difficulty in translating an image of the part tested on to a diagram which can show only two planes of space. We found that this difficulty disappeared when the diagram was replaced by the corresponding part of another individual. The part to be tested, for instance the left hand, is hidden from the patient by a screen, while the left hand of one of the observers is presented to him placed in a position as similar as possible to that of his own limb. On this living model of his hand the patient indicates with his other forefinger the exact spot on which he believes he had been touched. The second observer marks on a diagram the spot that is touched, together with the spot indicated by the patient, and thus a permanent record is obtained. When one hand is seriously paralysed the patient must usually withdraw the normal hand from behind the screen, when control observations are being made on it, in order to point to the spot that had been stimulated.

Occasionally we have also used the method in which the patient names the spot stimulated. But accurate results cannot be obtained by this method and it labours under the serious disadvantage that confusion frequently arises in the terms employed to designate the different parts, such as the fingers or their segments.

The groping method is useless as a means of testing the power of localization, as the results obtained by it are influenced by any disturbance of the power of recognizing the position in space of the part tested.

(3) *Roughness.*

The threshold for the appreciation of roughness is most conveniently determined by the Graham-Brown æsthesiometer. This consists of a mass of brass with a polished surface from which a tooth may be projected by a graduated screw. The instrument is drawn firmly over the part to be tested, and after each application the tooth is projected further till the patient can recognize the roughness. When the threshold is normal this is generally apparent to the observer at the same time as to the patient, owing to the increased resistance that is offered to the movement of the instrument by the projection raking on the skin.

Throughout this work we have used the original form of the instrument with one projection rather than that with many projecting cylinders.

We have used for the same purpose emery- or glass-paper of different degrees of roughness. We have adopted five grades and employ as a control a piece of smooth cardboard of the same thickness. The normal fingers, when drawn over the rough surface, can recognize even the finest emery-paper we employ as rough, and can easily distinguish the relative roughness of any two grades. When this faculty of sensation is affected the finest grade that can be recognized as rough represents the amount of the defect. This is a useful test, for by it the power of discriminating the relative roughness of two grades tested in succession may easily be determined.

(4) *Tickling and Scraping.*

The conclusions to which our investigations have led made it necessary to seek stimuli which are largely affective, or which contain a considerable affective component. Apart from pain, it is difficult to obtain a stimulus of this kind, but tickling unquestionably evokes a sensation which is strongly affective and may be either pleasant or unpleasant. The easiest method to produce tickling is to draw the pulps of the fingers gently over the soles of the feet; in some cases this stimulus also tickles the palms of the hands. In certain persons a wisp of cotton-wool rubbed gently over hair-clad parts produces tickling, especially over the pinna, on the neck and on the hair behind the ears, although in many such a stimulus is entirely ineffective for this purpose.

Scraping with the finger-nails is also a definite affective stimulus of the unpleasant order, as may be seen in cases in which there is an exaggerated response to affective stimuli. In such patients it may produce an intensely unpleasant sensation.

(5) *Vibration.*

To test the power of recognizing vibration we have employed a heavy tuning-fork, beating 128 vibrations per second [C°]. The fork, when strongly vibrating, is placed on some part of the affected half of the body, and, if the vibration can be appreciated, the patient is requested to compare the sensation evoked with that he obtains when the fork is applied to the corresponding part on the normal side. Afterwards he is asked to indicate at once when the vibrations of the fork appear to cease on the affected part, and it is then immediately transferred to the corresponding point on the normal side; the addi-

tional period during which it can be appreciated on this side, gives a measure of the reduction of sensation to this test on the affected half of the body.

(6) *Compasses.*

The ability to discriminate two simultaneous contacts may be tested by means of any of the forms of clinical compasses; we have found an ordinary carpenter's callipers with rounded points the most satisfactory.

The compass-points are set at a distance from one another which is just above the threshold on the normal side, that is to say, at such a distance that the patient has no difficulty in recognizing the two contacts when the points are applied simultaneously. Ten single and ten double contacts are then made in irregular order on the normal side, and the results are recorded by the method suggested by McDougall, and described by Rivers and Head [33]. Then the similar part on the affected half of the body is tested in the same way, with the compass-points set at the same distance from one another. If this is found to be below the threshold, the points are separated until a threshold can be obtained, or, if this is not possible, a record is taken with the compasses separated to a distance many times greater than that at which a perfect reading was obtained on the normal side (cf. p. 239).

But in addition to testing the ability to discriminate two points simultaneously applied in the ordinary way, we have found it necessary, when dealing with sensory disturbances from cerebral lesions, to investigate the power of recognizing two points applied to the skin in close succession. This can be carried out by bringing down first one point and, whilst it remains in contact with the surface, rapidly placing the second point upon the skin. Evidently, the interval of time between the successive applications must be short if the two points are to be appreciated as a double contact, and not simply as two successive touches. The following record, obtained from the affected forearm in a case where the power of recognizing the double nature of the compass-points was lost, whether they were applied simultaneously or successively, illustrates the method by which we record the results of this test:—

15 cm.	{	1	1 1 1 1										1 1 1 1 1 1				
		2	x x x x										x x				
		2 +	x x x										x x x x				

Here the compass-points were separated by a distance of 15 cm., and the contact of one point was recognized in every case correctly. But two points applied simultaneously (2) or successively (2+) were never said to be anything but one.

(7) *Pain.*

(a) *Superficial pain.*—Sensibility to pain may be tested first by pricking with a sharp steel pin or needle; the reaction to the prick should be observed, and the patient asked to compare the sensations he experiences when normal and affected parts are pricked in close succession. It must be remembered that even in this simple test there is a danger of confusion, as the contact of a point, in addition to evoking pain, gives an idea of "sharpness" due to the appreciation of the relative smallness of the stimulating object. Consequently, if the power of recognizing relative size is disturbed, the prick of a pin may be described as "less sharp" on the abnormal parts, although the pain evoked may be as great, or even greater, than on the normal side. It is therefore necessary to insure that the patient distinguishes between the sharpness of the stimulus and the pain or soreness it produces. Unhappily, this is often difficult, and consequently care must be taken to guard against this source of error before deciding that sensibility to pain is disturbed solely on the ground that pricks are described as "less sharp" than over normal parts.

If the loss is slight, such a conclusion can be satisfactorily attained only by determining the threshold for pain. The simplest instrument for this purpose is that which we have described as the pressure-æsthesiometer (fig. 5), with the contact disc removed so as to leave a naked point. The weight that must be placed on the needle before its contact evokes pain can be easily determined, and represents the threshold-value. This weight will vary with the sharpness of the needle, but by employing sewing needles of a definite grade, which can be attached to the steel rod, a standard of sharpness may be obtained. In our work, however, this was not essential, as we have always had a normal side with which to compare the pain-sensibility of the affected parts.

This simple instrument suffers from the disadvantage that it must be applied vertically. We have consequently employed, as a rule, another form of algesimeter (fig. 6). It consists of a metal tube (A) about 15 cm. in length, closed at one end and containing at the other

a piece of vulcanite (B), flattened at its projecting end and perforated to allow the projection of a needle (C). The tube contains a long needle, or a fine steel rod, to one end of which a needle may be attached. A fine spiral spring is fixed to the blunt end of this needle and the other end of the spring is inserted into a small bar (F) which projects into the tube through a slit ($a...b$) in one side of it, and is carried on a collar (E) that runs on the outer side of the tube. The spring is so arranged that it exerts no traction on the needle when the collar is at the highest point of the slit, and if the instrument is then applied vertically the point of the needle bears its own weight only. If, however, the collar is slid down towards the point of the needle tension is put on the spring and exerts a corresponding pressure on the needle. By measuring this on a balance the instrument can be graduated according to the pressure in grammes exerted on the needle when the collar stands at different points of the scale. An instrument graded between 2 grm. and 10 grm. is sufficient for ordinary clinical purposes. When the instrument is used horizontally or with the point upwards these values vary according to the weight of the needle, but this variation can be easily calculated. When, however, as in our work, it is sought to obtain a relative or comparative rather than an absolute threshold this point is unessential, if the instrument be applied at the same angle to the corresponding points of the two sides of the body.

It has been always recognized that it is difficult to obtain an accurate threshold for painful prick; for if a pin be applied with the same moderate pressure twice in succession to the same part, one contact may be appreciated as pain and the other as touch, depending largely on whether a pain-spot is directly stimulated or not. We consequently apply the algesimeter a certain number of times in close succession to the part to be examined, asking the patient to say whether he appreciates a prick or merely a touch, and take the reply for this series of stimulations instead of for each individual one.

We have found the faradic current an unsatisfactory means of measuring sensibility to pain at the higher levels of the nervous system and have not used it in this research.

(b) *Pressure-pain*.—For the measurement of deep pain we have used the modified Cattell's algometer, by which the amount of pressure on a standard area, necessary to evoke discomfort or pain, can be measured. Three or more readings are taken on each part, and the results are deduced by comparing the average obtained on the two sides. This is the more important as the amount of pressure with this

instrument, necessary to cause pain, varies with each observer, and although the actual numbers obtained by one may not be identical with those of another; a comparison between the results on the normal and abnormal side brings out remarkably similar results.

(8) *Temperature.*

To examine thermal sensibility we have used silver tubes 1.25 cm. in diameter. These are filled with hot or cold water and the temperature at the moment of testing it is read off on a thermometer; silver conducts so well that the temperature of the water and of the surface of the tube are almost identical.

First of all we determine the threshold for heat and for cold on similar parts of the two halves of the body, and consequently the range of the neutral zone on the two sides. Occasionally it may be advisable to make a further series of observations after the part to be tested has been adapted to heat or cold by placing it in water at different temperatures.

Then the power of distinguishing the relative warmth or relative coldness of two tubes, each of which can be recognized as warm or cold, is estimated and controlled by similar observations on the normal side.

Finally, we observe the effect of extreme degrees of heat and cold, such as 50° C. and above, or 15° C. and below, and compare the sensations they evoke on normal and abnormal parts.

Thermal stimuli form a ready method of applying a measurable affective stimulus; extreme degrees of heat and cold are uncomfortable or even painful, and warmth is usually distinctly pleasant. To study this affective component it is generally advisable to apply the stimulus to a larger area than that covered by one of our ordinary silver tubes; we have therefore employed for this purpose large glass tubes, measuring 4 cm. in diameter, filled with water at various temperatures.

These tests for thermal sensibility, simple as they may seem, are beset with difficulties and they are liable to lead to erroneous conclusions. One source of error is the tendency to call all sensations from affected parts, evoked during the testing, either hot or cold. Thus, although the patient is capable of no thermal appreciation, hot and cold tubes, or even repeated pricking, may be indiscriminately called "hot." This confusion is particularly liable to occur in cases where a lesion of the optic thalamus has led to an over-response to affective stimuli.

Moreover, it is not always easy to determine the extent of the neutral

zone, as most patients possess no word which expresses a neutral sensation. Before we begin testing with this purpose we therefore suggest that the answer shall be "warm touch," "cold touch," or "nothing but a touch." At the same time we compare the sensation evoked by the neutral temperature with that of a distinctly warm or cold tube.

(9) *Position.*

The power of recognizing the posture of any part of the body is tested in the usual way by placing a segment of a limb in some position and asking the patient to indicate, either by description or by imitation with the sound limb, into what position it has been placed. A second method is to ask him to touch with the normal hand some definite spot, such as the tip of the index-finger or of the great toe; this is a convenient test for knowledge of the position of the limb as a whole, especially if the faculty of localization is intact. The power to succeed in this test may be influenced by a defect of the sense of position at any joint of the limb.

As the ability to recognize the position of the limb may be aided by the memory of the passive movement by which its present position was reached, it is advisable in examining cases in which the loss is slight to obviate this factor as far as possible. This may be done by keeping the patient's attention diverted from the movement by conversation or questions, and by allowing the limb to remain in the position to be tested for a short time before his attention is directed to it.

A measurement of a defect in the sense of position may be obtained by the method introduced by Horsley [14], but for this purpose it is necessary that the opposite limb should be normal. Horsley employed a glass plate graduated into half-centimetre squares which could be placed, screened from the patient's sight, in any of the three planes of space. Instead of this glass plate, we have used a sheet of stiff cardboard, on one side of which a small depression is made to receive the tip of the index-finger of the limb to be tested, while to the other side a sheet of white paper can be fastened. This cardboard is placed in any position and the patient is required to bring the normal index-finger towards the tip of its fellow which lies on the opposite side; the spot on which it impinges on the paper is marked by the observer. A series of ten successive observations is made in this way. The sheet of paper can be then removed from the cardboard plate and forms a

permanent record of the amount and direction of the error, which when it is abnormal can be dependent only on the defective sense of position in the limb that remains at rest, if the moving limb is unaffected.

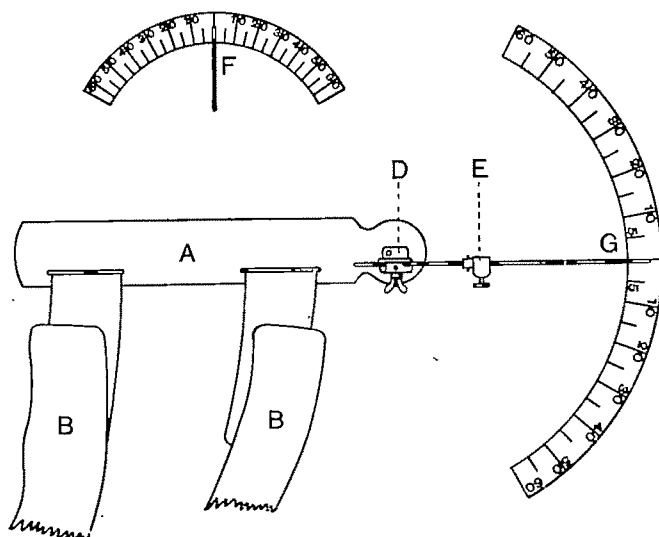


FIG. 7.—The instrument used by us to measure the extent of the smallest appreciable passive movement. The finer divisions of the scale are not shown upon this drawing for the sake of clearness.

(10) *Passive Movement.*

The power of appreciating passive movement may be roughly tested by changing the position of a segment of the limb and requiring the patient to indicate when he can appreciate the movement, and by noting the range necessary in order that its direction should be rightly perceived. In doubtful cases or where the defect is small it is always necessary to carry out control experiments on the opposite limb.

In order to measure the angle through which a movement must be made to be appreciated we employ a simple instrument (fig. 7) which consists of a long narrow plate of brass (A), lined with cloth, that can be strapped on to any part of the limb by bands (B) attached to it or held in contact with it by the observer. At one end of this plate an arm, which carries an arc of a circle with degrees marked on it, is attached by a joint (D) movable in all directions. Two such arcs can be adapted to our instrument, either of which can be attached at (E); one (F) with a radius of 7.5 cm. for measuring movements of shorter segments, as those of the fingers, and another (G) with a radius of

15 cm. for longer segments. The brass plate is applied to the limb in such a way that the point (D) lies immediately over the joint at which the movement is to be measured, and the arc is then brought into the plane of the movement that is to be made. The range of movement necessary for appreciation can be then easily read off from the scale on the arc.

We have also occasionally used a modification of the instrument designed by Goldscheider [10] for this purpose.

There are certain sources of error in obtaining such measurements. In the first place, the patient may reply when he feels the pressure of the observer's fingers by which the passive movement is made; but this can be easily obviated by grasping the part to be moved so firmly on two opposite surfaces that the additional pressure necessary to produce the movement cannot be distinguished. The part should be grasped between the fingers applied to the surfaces that lie in the plane in which the movement is to be made rather than on the surfaces vertical to the plane of movement, for then the dragging and displacement of the soft tissues may enable the patient to reply correctly, though he cannot appreciate the actual movement.

In the second place, the rate of the passive movement may influence its appreciation. To obviate errors from this source we have attempted to make the movement at a certain uniform rate, and, as our measurements have been always considered in relation to those obtained from the opposite sound limb, this safeguard is sufficient.

Finally, in a normal limb, a passive movement is appreciated, and its direction is recognized almost simultaneously; but, when the appreciation of passive movement is affected by a cerebral lesion, a much larger range of movement may be required in order that the patient may obtain a knowledge of its direction, than that which enables him to recognize its occurrence. It is therefore necessary in some cases to measure both separately.

(12) *The Appreciation of Weight.*

To test the appreciation of weight we have employed circular discs of lead 3 cm. in diameter, ranging from 20 grm. to 200 grm. in weight. The surface of each disc, which is placed in contact with the body, is covered with chamois leather, in order to prevent the coldness of the metal affecting the skin. This has the additional advantage that when the weights are placed one on the top of the other they have less tendency to slip.

With these weights we carry out the following series of tests, both with the hands fully supported and also when the patient is permitted to estimate the relative weight by "weighing"—i.e., by raising and lowering his hands.

(a) *With the hand supported.*—Two weights are placed successively on the normal hand, and the patient is asked to say which is the heavier. With weights, of the surface area we use, even the least intelligent can recognize the difference between 70 and 100 grm., and many can give a series of right answers with 80 and 100 grm. Two weights are found which can be correctly distinguished on the normal hand, and they are then employed to test the affected hand in the same way. Usually in our cases, if the power of recognizing weight was affected, the errors were gross, and in many instances no pair of weights could be found which could be distinguished with certainty. But, when the faculty of estimating relative weights was not completely lost, we were sometimes able to work out a true difference-threshold; that is to say, two weights could be found bearing to one another such a relation that one was always said to be the heavier, while another pair, which differed to a less degree, could not be distinguished. At least four observations are always made with each pair of weights.

Next we test the power of recognizing the increase or decrease of weight. For this purpose a thin cork disc of the same diameter as the weights is first laid upon the palm. To this progressively heavier weights are added, and then removed until the cork alone rests upon the palm. These weights are not added or removed in an unbroken sequence, but irregularly, and the patient is asked to indicate whenever any alteration in weight occurs. Thus the complete record of a series of observations might read as follows:—

Cork + 20 grm. + 30 grm. + 50 grm. — 50 grm. — 30 grm. + 30 grm. + 50 grm. + 100 grm

First of all the sound hand is tested, and the patient's normal capacity determined; then a similar series of tests is applied to the affected hand. When the power of recognizing addition or subtraction of weight is lost, the jarring produced by the manipulation may be appreciated; this tactile sensation, evoked by the act of removing one weight from, or adding it to another, is a fruitful source of error, but with care and practice can be reduced to a minimum. Moreover, by gently touching the weight which lies on the hand without altering it, we can ascertain whether the patient's replies are

due to recognition of a change in weight, or to the tactile stimulus evoked by the manipulations of addition or removal.

Finally, the patient is asked to compare two weights placed one on each fully supported hand.

(b) *With the hands unsupported.*—A weight is placed in each hand and the patient is asked to “weigh” them by raising and lowering his hands. Another method is to place a weight in one hand and then to substitute another one for it, each weight being raised and lowered several times. In normal persons the latter method gives the more accurate results, but our patients often became so confused on the affected hand by the absence of a normal standard that we have usually adopted the first form of this test.

(13) *Appreciation of Size.*

The ability to recognize differences in size may be tested by placing in succession two objects of different size but of the same shape in contact with the part, and asking the patient to distinguish which is the larger. By varying the relative size of the objects, a threshold for this form of discrimination can be obtained. For this purpose we employ circular pieces of thick leather increasing by half a centimetre, from 1 cm. to 4 cm. in diameter. Leather has the advantage that it is rarely cold to the skin, and pieces 4 to 5 mm. in thickness are sufficiently rigid for the purpose. Each disc is provided with a handle on one surface by which it can be manipulated with ease.

The appreciation of size is most conveniently tested on the palms, as there the difference-threshold is small.

The ability to distinguish the head from the point of a pin, when the latter is applied so gently that it does not prick, depends on the power of recognizing relative size.

(14) *Appreciation of Shape.*

By shape we mean the two-dimensional contour of an object that can be recognized on contact with the surface of the body. To test this faculty we have employed simple shapes, generally a circle, a square, a triangle and an oblong, cut out of stiff leather. In the set we have found most convenient each side of the square, the diameter of the circle, and the height of the triangle were all 3.5 cm., while the oblong was also of this length and 1.75 cm. in breadth.

The shape of these objects can be easily distinguished on the normal palm when they are applied firmly and evenly, but unhappily they can rarely be recognized on most other parts of the body, including the soles of the feet.

(15) *Form in Three Dimensions.*

We employ the word "form" to mean the three-dimensional shape of an object, and test the ability to appreciate it by placing objects in the patient's hand and asking him to determine their form by feeling them and by moving them about between his fingers. Any ordinary object may be employed for this test, but we have found it advisable to use in addition standard tests of geometrical form such as a cube, a cylinder, an ellipse (called by the patients "an egg"), a cone and a pyramid, made in approximately the same bulk from wood. The patient is first asked to select his own names for them, or if description offers any difficulty he is allowed to point to the object he identifies in a duplicate set before him.

When there is serious paralysis of the fingers, the test-object must be moved about by the observer in the patient's hand; we have found this sufficient with the objects we use when the ability to recognize form is not lost.

In addition to the power of appreciating form, we always test the patient's ability to recognize familiar objects placed in his hand with the eyes closed.

(16) *Appreciation of Texture.*

Interesting facts may be obtained by testing the patient's ability to recognize the texture of ordinary stuffs by touch. For this purpose we employ a set of common materials—calico, flannel, silk, cloth and velvet, which the patient is allowed to feel and move about between his fingers. Those we use can usually be identified with ease by the patient's normal hand.

(17) *Dominoes.*

Occasionally, more particularly in cases of cortical lesions, we have used dominoes made for the blind with pips raised from the surface. The patient's eyes are closed and he attempts to count the number of pips by passing his fingers over the surface.

(18) *Appreciation of Consistence.*

To test the power of recognizing the consistence or hardness of objects we employ a set of small pieces of rubber tube of the same diameter and with a similar surface. Some specimens have thinner walls than others, and in order to obtain firmer test-objects some are filled with substances of different hardness. They are numbered according to the resistance they offer to compression, and, when the patient has compressed two in succession between his forefinger and thumb, he is asked to say which is the harder, and the results obtained from the two hands are compared.

SCHEDULE FOR THE EXAMINATION OF SENSIBILITY.

(A) SPONTANEOUS SENSATIONS.

Pain. Numbness. Tingling.
Position of the limb. Idea of the limb.

(B) LOSS OF SENSATION.

(1) *Touch.*(a) *Light Touch.*

Cotton-wool on hairless and hair-clad parts.
Threshold with von Frey's hairs.

(b) *Pressure-touch.*

Threshold with the pressure-æsthesiometer.

(2) *Localization.*

Naming the part touched.
Henri's method, as modified by us.

(3) *Roughness.*

Threshold with Graham-Brown's æsthesiometer.
Sand-paper tests; discrimination of relative roughness.

(4) *Tickling and Scraping.*

Tickling on soles and palms.
Cotton-wool rubbed over hair-clad parts.
Light scraping with the finger-nails.

(5) *Vibration.*

Loss or diminution of sensibility.
Alteration in the character of the sensation evoked.

(6) *Compasses.*

Points simultaneously applied.
Points successively applied.

(7) *Pain.*(a) *Superficial Pain.*

Pin-prick.

Threshold with the algometer.

Reaction to measured painful stimuli.

(b) *Pressure-pain.*

Threshold with the algometer.

Reaction to painful pressure.

(8) *Temperature.*

Thresholds for heat and cold.

Effect of adaption on the threshold.

Discrimination of different degrees of heat and of cold.

Affective reactions : (a) to extreme degrees.

(b) to warmth.

(9) *Position.*

By imitating with the sound limb the position of the affected limb.

By pointing with the sound limb.

Measurement of the defect by Horsley's method.

(10) *Passive Movement.*

Appreciation of movement.

Recognition of the direction of movement.

Measurement of the angle of the smallest movement which can be appreciated.

Falling away of the unsupported limb when the eyes are closed.

(11) *Active Movement.*

Imitation of movement by the sound limb.

Ability to touch a known spot.

Measurement of the defect by Horsley's method.

(12) *Weight.*(a) *With hand supported.*

Recognition of differences in weights applied successively to one hand.

Appreciation of increase or decrease of weight.

Comparison of two weights placed one in each hand.

(b) *With hand unsupported.*

Comparison of two weights placed one in each hand.

Recognition of differences in weights applied successively to one hand.

(13) *Size.*

Difference-threshold.

Distinction of the head from the point of pin.

- (14) *Shape* (Two-dimensional).
- (15) *Form* (Three-dimensional).
Recognition of common objects by their form.
- (16) *Texture*.
- (17) *Dominoes*.
Ability to count points by touch.
- (18) *Consistence*.
- (19) *Testicular Sensibility*.
Light pressure.
Painful pressure.
- (20) Sensibility of the *Glans Penis* to measured prick.

APPENDIX II.

SHORT ACCOUNTS OF ILLUSTRATIVE CASES.

CASE 1.—*Brown-Séquard paralysis* (vide p. 110).

CASE 2.—*The consequences of a lesion of the brain-stem* (vide p. 114).

CASE 3.—*Occlusion of the posterior inferior cerebellar artery* (vide p. 117).

CASE 4.—*Tumour of the mid-brain and optic thalamus* (vide p. 121).

CASE 5.—*Disease of the optic thalamus* (vide p. 126).

CASE 6.—*Disease of the optic thalamus with autopsy* (vide p. 127).

CASE 7.—*An instance of the thalamic syndrome with scarcely any loss of sensation.*

Rachel F., aged 60, was admitted into the National Hospital under the care of one of us (G. H.) in February, 1910. She was a married woman and had enjoyed good health till September, 1908, when the stroke occurred that produced her symptoms. While engaged in her housework, she suddenly experienced a "peculiar drawn feeling" in her left shoulder and the left side of her neck, and then fell to the floor, but did not lose consciousness. She immediately lost the power of moving her left limbs and felt as if these limbs had disappeared, "as if I had lost them." She soon discovered that she "could not feel" on these limbs or on this side of her body.

After a period of about five or six weeks she began to move the left limbs again; three months after the stroke she was able to walk alone, and a little later she could bring the left hand to her mouth. Since then the affected limbs have become gradually stronger. About six months after the attack she first noticed the irregular spontaneous movements of the left hand, which, though very variable in intensity, have on the whole increased. A little later similar movements of the left toes became noticeable.

The "peculiar drawn feeling" that ushered in the attack probably persisted for a few weeks; on this point her memory is indefinite, but as sensation returned she began to complain of an "unpleasant numb feeling" and of tingling and "pins and needles" in the left hand and arm, and of numbness in the left foot. About six months after the onset she began to have a sensation as if "something were crawling under the skin" of the affected side, especially on her face, and a "scalding sensation in the left cheek, which is worse when the cheek is cold than when it's warm." For about the same length of time she has suffered with dull aching pains in her left arm, and a "crampy pain" in the left leg.

Vision, hearing, smell and taste were, as far as she knows, unaffected by the attack, but the left side of her mouth and tongue "have always felt dry," and food always seems rough and cold on this side; even a cup of hot tea is unpleasantly cold to the left cheek.

Speech and swallowing were never affected; during the first few days of her illness she had slight difficulty in holding her urine, but this soon passed off.

CONDITION IN FEBRUARY, 1910.

She is a healthy-looking woman who appears much younger than her age. Her heart is slightly hypertrophied, her arteries rigid, and her pulse-tension high.

She is fairly educated and intelligent; her memory is excellent and her attention good.

Special senses.—Smell, taste, and hearing are unaffected and equally acute on the two sides. The visual fields are unrestricted and the optic discs are normal, but the retinal arteries appear sclerosed.

Cranial nerves.—The functions of all the cranial nerves are unaffected; the pupils are equal and react well to light and on accommodation. The corneal reflex is brisk on the right side, but very much reduced or almost absent on the left.

Motor system.—The right limbs are normal in every respect. The size and tone of the muscles are equal in the two arms and the range of movement of the left is unrestricted, though this limb is distinctly weaker than the right; the grasp of the right hand, measured with the dynamometer, was 41 (an average of five readings), while on the left it was 23 only. She uses this limb readily in coarse general movements, as in pointing, but owing to the spontaneous movements and ataxia it is useless to her for finer actions. There are almost constantly irregular involuntary movements of the left fingers and frequently, too, of the wrist; they often constitute a rhythmical tremor, but are more usually irregular or even choreiform. The most common movement is flexion and extension of the fingers at the basal joints, but flexion and extension of the wrist and adduction and abduction of the fingers are also of frequent occurrence. These movements increase on any attempt to use the limb, on strong volitional movements of the normal arm and even on walking. They persist during the movement of the limb itself as a sort of intention-

tremor, but differ from an ordinary intention-tremor in that the amplitude of the oscillations is greatest when the movement is begun and decreases towards its completion. She has very little power of restraining the movements. In addition to the tremor there is considerable ataxia of the limb.

The movements of the trunk and head are unaffected.

There is no wasting or alteration in the tone of the muscles of the left lower limb, and its movements are only slightly weaker than the corresponding ones of the right limb. Spontaneous movements, more or less similar to those described in the arm, occur in the left toes and at the ankle, and the volitional movements of this limb are poorly co-ordinated and tremulous. She walks with short shuffling steps, occasionally dragging the left toes along the ground. Her gait is more affected than might be expected from the relatively slight weakness of the leg.

Reflexes.—All the tendon-jerks are brisker on the left than on the right side. The abdominal reflexes cannot be obtained on either side. The right plantar reflex gives a flexor, but the right an extensor response.

Spontaneous sensations.—She complains chiefly of a "scalding sensation" and of burning pain in her left cheek. The left side of her mouth and this side of her tongue are dry, rough and sore, and it seems to her as if this side of her palate were "covered with ulcers." All food, no matter what its temperature may be, is unpleasantly cold to this side of her mouth. She also complains of "aching pains" in the left shoulder and the left arm (there are no arthritic changes) which are often so severe as to keep her awake, and of "crampy pain" in her left leg, especially behind the knee. The left hand and foot are usually numb and the hand often tingles.

Tactile sensibility.—She appreciates light cotton-wool contacts equally well on the two sides, on both hairless and hair-clad parts, and can recognize no difference in the sensations evoked. On testing with von Frey's hairs the same threshold is obtained on both hands and on the cheeks. It was noticed, however, that after the left cheek had been tested she rubbed the spot on which the contacts with the hairs had been made, and when asked why she did so said, "You made it itch and tingle"; the tingling persisted for some time after stimulation.

Roughness.—With Graham-Brown's instrument the same threshold for roughness was obtained on the two sides, but when a stimulus above the threshold is employed it appears rougher on the affected than on the sound side, and especially on the sole produces a more violent movement of withdrawal.

Tickling.—This can be evoked satisfactorily from the soles only. The left sole is very much more ticklish than the right, and stimulation by drawing the fingers across it produces a strong vigorous reaction and rapid withdrawal of the limb, while on the right side this evokes scarcely any emotional reaction. The tickling of the left side is not, however, actually painful or unpleasant.

Vibration.—There is a shortening of the period during which vibration can be appreciated on the left hand compared with the right, and the vibrations of the fork appear "plainer" on the normal side.

Sensibility to pain.—No diminution of sensibility to pricking can be detected on any part of the left side, and with both the spring and pressure-algesimeters the thresholds are found to be identical on corresponding parts. Pricks that evoke pain, however, are invariably "sharper," more unpleasant and "sting more" on the affected than on the normal side, and in many places, especially on the palm and sole, produce a much greater reaction with an apparently uncontrollable tendency to withdraw the part. On testing with the algesimeter this is found to occur with any stimulus above the threshold. There is no evidence that the pain persists abnormally, or that it radiates from the spot stimulated.

Pressure-pain.—As measured with the algometer the threshold is approximately the same on the two sides, or in places, as on the sole, actually lower on the affected side.

			R.			L.		
Palm	..	..	5½	6	7	5½	6	7
Tibia	..	..	8	2	2½	2½	2	2
Sole	..	..	5	5½	5	8½	2½	2½

But painful pressure on the affected side evokes a much greater reaction and appears to the patient "very much sorer" and more painful. When such pain is produced on the right sole, for instance, only a slight jerk of the leg occurs, while on the left side the foot is dorsiflexed violently and the leg is drawn up and her general response denotes intolerable discomfort.

Thermal sensibility.—All degrees of temperature can be normally appreciated on both sides and the thresholds are equal; but extreme temperatures, as ice and tubes above 55° C., appear to her colder or hotter on the left side, and evoke stronger reactions.

Sense of position.—There is slight loss in the left arm, especially at the distal joints, but none can be demonstrated with certainty in the leg.

Appreciation of passive movements.—By ordinary methods of testing there seems to be very little alteration in the affected arm, but by measuring the angle of movement necessary for its appreciation and the recognition of its direction a definite defect is revealed. The following records were obtained on moving the index-finger at its basal joint:—

R. Index-finger	..	Flexion	2½ 2			2 2 2		
	..	Extension	2	2	1½	1½	2	
L. Index-finger	..	Flexion	10 12 12			15 12		
	..	Extension	7½	10	6 7 8			

Localization tested on the hands is found to be equally accurate on the two sides.

Compasses.—The threshold is approximately the same on the two sides, and she is equally quick and decisive in her replies from the two sides. A perfect series of readings can be obtained with 1.5 cm. on the palms and with 2 cm. on the soles.

Appreciation of weight, tested by the different methods we employ, seems almost as accurate on one side as on the other. She is less easily able to

recognize alterations in weights lying on the left than on the right hand, but the constant involuntary movements of the affected hand make this test difficult.

Appreciation of size.—The same difference-threshold is obtained for the two hands.

Appreciation of shape and form.—There is no material difference between the two hands to these tests, though she is a little slower and less certain in recognizing differences in shape on the left than on the right.

Recognition of relative consistence.—She frequently fails to recognize the relative hardness of two test-objects placed in the left hand, which she can easily distinguish in the right hand.

Recognition of texture.—With the left hand she fails to recognize the texture of many of the test-stuffs we placed in it. Silk, for instance, is called cotton, velvet was described as woolly or something rough, and cotton as a woollen material.

She has remained under observation as an out-patient at the National Hospital since these notes were taken in an unchanged state, excepting that she complains more of the pains in the left side. The observations recorded above have been repeated and verified on many subsequent occasions.

CASE 8.—An instance of the thalamic syndrome where cutaneous sensibility was not diminished. All pleasant or disagreeable stimuli, more particularly heat and cold, produced a profoundly greater response on the affected half of the body.

George S., aged 64, was admitted into the National Hospital under the care of one of us (G. H.) in September, 1910. He was well till the attack, that produced his symptoms, occurred in February, 1909. While walking he noticed a numbness in his left cheek and his left hand, and a few hours later a tingling, "like pins and needles," spread over his left arm and from his shoulder into his face; it was particularly severe in the left side of his tongue. Later in the day the tingling extended throughout his left side and into his left leg; then he had some difficulty in walking. He was kept awake that night by a soreness and painful tingling in his left arm, which next morning was present over his whole left side. He never lost the power of moving the affected limbs, in fact their movements were scarcely limited, and there was not much diminution of sensation on this side: "I was able to feel everything, in fact too much so"; but objects he touches have not felt natural since the attack. The pains and uncomfortable sensations have persisted more or less unaltered from their onset, but they have always been worse in either very hot or very cold weather.

Hearing and vision were unaffected, but he has found that he cannot taste so well since his illness; he noticed this loss of taste the day after the onset. He complains, too, that his mouth has become very dry. During the past year he has occasionally had a slight tingling pain in his right hand and a "tingling numbness" in the right leg, but, unlike the paræsthesiæ on the left side, these sensations are not constant.

CONDITION IN SEPTEMBER, 1910.

He is a thin, spare man, but fairly well preserved for his age. His arteries are rigid and the pulse-tension high, but there is no other sign of visceral disease. He had been an engineer and is fairly well educated; his memory and attention are excellent.

Special senses.—Smell is unaffected. He cannot taste sugar or salt on either side of his tongue, but quinine can be appreciated equally on both sides. There has been for years considerable middle-ear deafness on the left side, but there is no other demonstrable affection of hearing. Vision is poor owing to commencing cataract, but the visual fields are unrestricted.

Cranial nerves.—The functions of all are unaffected, except that the left corneal reflex is very much diminished.

Motor system.—The right limbs are unaffected. There is a slight general wasting of the small muscles of the left hand, but otherwise the right and left limbs are equally developed. The tone of the two sides is about equal, and there are no contractures. The left arm is slightly weaker than the right, but this is largely due to the fact that strong muscular contractions give pain. Its movements are also slower and more awkward. Involuntary movements do not occur.

Reflexes.—The tendon-jerks and the abdominal reflexes are equal on the two sides, and both plantar reflexes give definite flexor responses.

Spontaneous sensations.—He complains of a constant "soreness" of his left hand and his left foot, and of similar pain in the left half of his tongue. The whole of the left side also "feels cold," and anything that touches it seems unpleasantly cold to him. He always wears a glove on this hand. The whole of this side is also tender; when he places his foot on the ground, for instance, "it feels as if there were tacks under the foot." He also complains of "a painful tingling," throughout this side, of a "gnawing pain" in the left temple, and occasionally "sharp pains" shoot through the left limbs.

Tactile sensibility.—Light cotton-wool contacts are equally well appreciated on the right and the left sides, and there is no obvious difference in reaction to this stimulus. The same threshold can be obtained on the two sides with von Frey's hairs.

Roughness.—The same threshold is obtained with Graham-Brown's instrument on the two sides, and no over-reaction or expression of discomfort is evoked from either palm or sole.

Tickling and scraping.—There is no over-reaction to tickling, and he says there is very little difference between the sensations evoked on the two sides. The left side of the body is, however, more "tender" to scraping than the right.

Vibration is equally well appreciated on the two sides, and the fork evokes no unpleasant sensations on either side.

Sensibility to pain.—The left limbs and the whole of the left half of the body, including this side of the face and tongue, are "more sensitive" to pricks

than similar parts of the right side, and the reaction thereto and the emotional expression are considerably greater. When a pin is drawn across his chest from the right to the left side he immediately complains that it is more painful to the left of the middle line. As measured with the algesimeter there is no difference in the threshold on the two sides.

Pressure-pain.—The algometer produces intolerable pain on the left side, and a sudden and violent reaction. As soon as pain is evoked he writhes and jumps; moreover, its effects persist longer than on the right side. The threshold-values, too, are distinctly lower on the affected side.

	R.				L.		
Palm	7	7	7	..	5½	5	4½
Second metacarpal ..	5	4	4	..	2½	2	2
Sole	8	2½	2½	..	1½	2	1½

Thermal sensibility.—There is no diminished appreciation of temperature over the affected half of the body, and the same thresholds for heat and cold were obtained on the two sides. But any temperature that is definitely cold to the left side causes an expression of discomfort and an excessive reaction; a tube a few degrees below the threshold is "just cold" to the right hand, but "very cold, very unpleasant" to the left. Similarly, even 45° C. which was described as warm on the right hand, was "too hot and uncomfortable" on the left. When, however, milder degrees of warmth, as 38° C., are employed, or if the hands are placed on a vessel containing water at this temperature, he describes the sensation evoked in the affected hand as "delightful," or "more soothing and more pleasant than on the right." Further, he states that this gives him not merely local pleasure, but "makes him feel happy all over," and this is clearly indicated by his general reaction and expression.

The thresholds were afterwards carefully determined for the two hands; 28° C. was neutral to both, while 30° C. was "warm" to the right and "nice and warm" to the left. The hands were then adapted to warmth by being placed in a warm bath at 42° to 43° C. for two and a half minutes, and were tested again to the same temperatures immediately on removal. Now 28° C., which was previously neutral, was "very cold, very unpleasant" to the left hand, and 30° C., which had been "nice and warm," was either neutral or "just cold." Thus, by adaptation, the thresholds for heat and cold were easily shifted, and 28° C., which had been neutral, received a feeling-tone of discomfort, while 30° C. lost its feeling-tone of pleasure and became neutral.

Sense of position and the appreciation of passive movement.—There is considerable loss of the power of recognizing the position of his left limbs, which is greater at the distal joints; he is, for instance, unable to describe or to imitate with his right hand the positions into which his left hand or fingers may be placed. The appreciation of passive movement is also affected; in order that a movement of the left fingers can be recognized it is necessary that its range should be about four times as great as that required on the

right hand, and at the elbow the range of movement must be three to four times as large as on the right side.

The power of *localization*, the *compass-test*, and the recognition of *size*, *shape*, *form* and *consistence* are equal on both sides, and remarkably accurate.

Appreciation of weight.—When the hands are supported the appreciation of weight is little different on the two sides; two weights placed consecutively on the same hand can be discriminated within about the same limits on the two sides. When, however, the hands are unsupported he fails to recognize the difference between 50 gm. in the right hand and 200 gm. in the left. These observations are rendered difficult by the tendency for the sensation of weight to die out when the test-object is allowed to lie for any time in the affected hand.

Thus it would seem that, in this case, the power of estimating weight on the unsupported hand was dissociated from the faculty of estimating relative pressures when the hands are fully supported.

CASE 9.—*An instance of the thalamic syndrome where the thresholds to painful stimuli were identical on the two sides, and heat produced excessive pleasure on the affected half of the body.*

Peter C., aged 59, was admitted to the Seamen's Hospital under the care of one of us (G. H.) in June, 1911. In December, 1909, he noticed he was unusually thirsty and that the amount of urine he passed was greatly increased; his doctor told him it contained sugar, and put him on a restricted diet.

On March 20, 1910, he went to bed well, but woke in the early morning to find that his left limbs were paralysed. He remained several weeks in bed, but was able to walk again in about three months. Shortly before the stroke he found that his sight was affected and he could "scarcely see anything on the left side." There was no diplopia.

At first the left limbs were paralysed, but, as power returned, he noticed that he had difficulty in controlling their movements; he cannot say exactly when the involuntary movements of the left hand began. He thinks that the numbness, tingling and pains, from which he now suffers on the left side, came on immediately after the attack, but the pain was certainly less in the earlier stages than it is now.

CONDITION IN JUNE, 1910.

He is a somewhat old-looking man for his years, with degenerated arteries and a high-tension pulse. His urine is of high specific gravity, greatly increased in amount, and contains much sugar but no albumen. He is an intelligent, well-educated man and had been an overseer in his work. His memory is fair and attention good.

Special senses.—Smell, taste and hearing are unaffected, but there is complete left hemianopsia, the blindness reaching up to within three degrees of the fixation point.

Cranial nerves.—The functions of the cranial nerves are unaffected, except that the corneal reflex of the left side cannot be obtained.

Motor system.—The right limbs are entirely unaffected. There is no rigidity of the left arm and leg, and no loss of voluntary power, but all their movements are gravely ataxic. In addition there are almost constant involuntary movements of the arm, which generally take the form of a tremor, but at times are more irregular or choreiform.

Reflexes.—The tendon-jerks are present and equal on the two sides, ankle-clonus cannot be obtained, and the plantar reflexes are of the flexor type.

Spontaneous sensations.—He complains of pain, tingling and numbness in the left half of the body. The pain has the character of a dull aching, "as if bruised from a blow." The tingling is mainly in the left hand and foot and is constantly present. He describes the numbness as "a sort of dead pain" which occupies the whole of the left half of his body, except the face, and is much worse in cold weather.

Tactile sensibility.—He fails to appreciate many contacts of cotton-wool when it is rubbed over the hairless parts of the affected side, such as the palm and the sole, but he almost always succeeds in recognizing this stimulus on hair-clad parts of the body. When asked to compare the sensations evoked on the two sides, he says that the cotton-wool is more distinct over the normal palm and sole, but on hair-clad parts the sensations are "sharper and heavier" on the affected side. On testing with von Frey's hairs the threshold was found to be slightly raised on the affected side: on the normal hand a hair of 21 grm./mm.² was appreciated perfectly, while on the opposite hand 35 grm./mm.² was required to produce a sensation.

Roughness.—It is impossible to measure the power of appreciating roughness, for even the smooth surface of Graham-Brown's instrument produces a sensation on the left side which he cannot distinguish from that of roughness; but, when the instrument, set at the same degree of roughness, is rubbed over the two hands, he says it seems rougher on the normal, but more unpleasant on the affected side.

Tickling and scraping.—Gentle stimulation of the normal sole with the pulps of the fingers produces a tickling which is not unpleasant, but on the affected sole this stimulation is disagreeable and evokes an excessive reaction. This difference is still greater when the soles are scraped.

Vibration.—The vibration of a tuning-fork can be appreciated on the left side, but it is distinctly shortened as compared with the right side. It evokes no excessive reaction.

Pain.—There is no evidence of diminished sensibility to prick on the affected side, and the algesimeter gives identical threshold-values on the two halves of the body. But when two pricks of equal value are compared on corresponding parts of the two sides he invariably says that on the affected part "it hurts more and is three times as sore"; moreover the reaction evoked is much greater than that from the normal side. He says, "I can't stand it so well on the left side: the pricks seem to stay there they don't go away when you take away the pin."

Pressure-pain.—As tested with the algometer the threshold-values are approximately the same on the two halves of the body, but the reaction to this stimulus is everywhere greater on the left side than on the right.

Thermal sensibility.—There is a slight reduction of sensibility to temperature on the left half of the body. Thus temperatures between about 25° C. and 40° C. are not appreciated, whilst the neutral zone on the normal side extends from 28° C. to 33° C.; the extremes of temperature produce more disagreeable sensations and a greater emotional reaction on the affected side. But when large tubes containing water at 40° C., or slightly above, are applied to the affected parts of the body he says, "That's nice, it's much more pleasant than on the other side." Even when warm hands are placed on his hands or on his feet, he says that the sensation is different on the two sides; on the affected half of the body "it is more comfortable; it is a real pleasure; it soothes me; it gives me the feeling that it must do me good." At the same time his face lights up with a definite expression of pleasure.

Sense of position.—The knowledge of the position of the distal joints of the left arm and leg is defective, but there is less loss at the proximal joints.

Appreciation of passive movement is defective in the left hand as compared with the right; the fingers must be moved through nearly ten times as great an angle as is necessary on the right side before the movement can be appreciated. At the elbow the loss on the left side is considerably less in proportion: he can appreciate a movement that is not more than three times as great as that necessary on the normal side.

Compasses.—The compass-test is gravely affected on the abnormal half of the body: good readings are not obtained even when the points are separated to 5 cm. on the palm, or to 15 cm. on the forearm. He has no difficulty, however, in recognizing the two points when applied successively.

Localization is perfect on both sides.

Appreciation of size is somewhat defective in the left hand: thus he failed in every case to recognize the difference between objects with diameters of 3·5 and 4 cm., and of 2 and 2·5 cm., although he was uniformly correct on the normal side; but as soon as the difference was increased to that between diameters of 3 and 4 cm., or 2 and 3 cm., his answers from the affected hand are uniformly correct. It is therefore possible to obtain a definite difference-threshold for the appreciation of size.

Shape, form, texture and consistence are all badly appreciated when the tests are applied to the left hand.

CASE 10.—*An instance of the thalamic syndrome associated with complete loss of thermal sensibility, although hot and cold stimuli produced pleasure and discomfort.*

Margaret B., aged 65, was seen at the West End Hospital for Nervous Diseases in July, 1911, through the kindness of Dr. Harry Campbell, to whom we are much indebted for the privilege of making the following observations. Her past health had been good; she married at 28 years of age, but has had no children.

In October, 1910, she suddenly found she was unable to hold anything in the left hand, and almost immediately fell to the floor unconscious. When she regained consciousness some hours later she was unable to move her left limbs, and they, together with the left side of her trunk and face, seemed numb: at first it seemed to her that she had completely lost her left arm. About six weeks later some power of movement returned in the arm, and in two months she was able to walk with a little assistance. Since then she has improved gradually; walking has been her chief trouble, as owing to its tenderness she cannot place the left foot properly on the ground. The involuntary movements of the left arm began as the power of movement returned; she is aware of them only when she sees them. About two or three weeks after the stroke the left-sided pains first appeared, as a gnawing pain in the groin; they increased in intensity during the first two or three months of her illness.

Vision, hearing, smell and taste were not affected, and she has not had any sphincter disturbance or affection of speech. Since the attack, however, she has noticed that her mouth is unnaturally dry.

CONDITION IN JULY, 1911.

A rather thin, elderly woman. She says she has lost much weight during her illness, and attributes it to the pains which disturb her day and night. She is intelligent, her memory is fair, and she is satisfactorily attentive when under examination.

Cranial nerves.—The functions of all the cranial nerves are normal: there is no difference between the voluntary or expressional movements of the two sides of the face, and the tongue is protruded straight. The pupils are equal, and react well to light and on accommodation. The right corneal reflex is brisk, but the left is absent.

Special senses.—Smell, taste, hearing and vision are normal, and the visual fields are unrestricted.

Motor system.—The right limbs are unaffected.

The muscles of the left forearm and hand are slightly wasted, but the tone of the limb is unaltered and there is no tendency to contracture. Movement is somewhat limited at the shoulder-joint by arthritic changes, but is otherwise unrestricted. Owing to the great loss of sensation it is difficult to estimate the actual strength of the limb, but there seems to be little, if any, weakness; she is slow, however, in exerting power on this side, and her efforts are not well sustained. All its movements are ataxic, and there is in addition considerable intention-tremor. While the arm lies on the bed frequent irregular involuntary movements of its distal segments occur. These generally take the form of a sudden extension of one or more fingers, or an isolated movement at the wrist, but often a short series of oscillations (tremor) may be observed. These involuntary movements can be excited or exaggerated by certain peripheral stimuli, even if they do not reach consciousness.

There is no definite wasting of the left leg, and the tone of its muscles is normal; there is no rigidity or contractures, and the range of movement is unrestricted. The power is almost as good as that of the right limb, but its movements are very ataxic. No involuntary movements have been seen in the leg. She walks with short shuffling steps as though she were afraid to trust her weight on the left limb.

Reflexes.—The arm-jerks are equal and brisk on both sides. The knee- and ankle-jerks are slightly greater on the left side, but clonus could not be obtained. The abdominal reflexes are absent. The right plantar reflex is flexor, but stimulation of the left sole provokes such an extensive and vigorous movement of the whole limb, and such dislike on the part of the patient, that the exact nature of the response cannot be determined; however, no typical slow extension of the great toe can be seen.

Spontaneous sensations.—She gives vivid descriptions of the pain and disagreeable sensations she suffers on the left side. "There is a feeling as if boiling water were being poured down the left arm from the shoulder to the elbow, and as if I had a band on the forearm which someone was pulling so tight as to hurt me." There is also a sensation at the back of the left shoulder "as if a log of wood were hanging from it." The hand is numb and feels "as if little pins were sticking into the fingers."

There is also pain in the left eye, "a tight feeling in the face," and "a feeling of fullness in the left ear." "I can't lie on the left side of my head as it is so sore." Pain is always present in the left side of her body, greatest above the iliac crest: "It feels as if you had your nails dug into my side and you were hanging with your whole weight on it," or "as if rats were always gnawing at my side." Her left thigh from the hip to the knee seems painfully tight, and below the knee there is a constant gnawing pain, greatest in the heel and the sole of the foot. She cannot lie on the left side as it is so tender, and cannot bear anything cold to touch it.

Tactile sensibility.—She fails to appreciate cotton-wool contacts on the left hand and fingers, and on the hairless parts of the rest of the limb. If, however, a wisp of wool is rubbed backwards and forwards on the hair-clad parts, as on the back of the forearm, an unpleasant sensation is evoked, "a curious tickling," which is unquestionably painful, or "a burning feeling as if you touched me with something very hot." Yet, over the same parts, she always fails to appreciate cotton-wool when merely pressed on, no matter how firmly. The condition is exactly similar on the left leg, and yet a very intense reaction can be evoked by rubbing wool on the sole. She can recognize most contacts on the left side of the face unless they are slight, and also on this half of her body. Rubbing a wisp of wool on the left chest provokes a strong reaction; she winces and afterwards rubs the part with her own hand, complaining that "you made it itch." When a wisp of wool was rubbed to and fro on the fingers curious involuntary movements began, yet she was conscious neither of the stimulation nor of the movement. This was repeatedly verified.

Pressure-touch was tested with the pulp of a finger that had about the same surface temperature as her own skin. She is unable to recognize firm pressure on the whole of the left arm and leg; even when some part of these limbs is firmly grasped she appreciates nothing, provided the pressure is not sufficiently great to give discomfort. She is also insensitive to moderate pressure on the left side of her face, and even the eyeball can be pressed firmly through the upper lid without arousing her consciousness.

Roughness.—She has lost the ability of appreciating roughness on the left side. On testing the palm with Graham-Brown's instrument it is found that, even when the surface is quite smooth, it produces an unpleasant tingling sensation; but she cannot distinguish this sensation from that evoked by the instrument when the cylinder is projected 10 degrees (0.5 mm).

Tickling and scraping.—She is naturally extremely ticklish. Drawing the tips of the fingers over the right sole tickles her greatly and evokes a strong reaction, but not an expression of discomfort, while on the left sole the same stimulation is unbearable, and she says: "It's burning; it's as if you were tearing the skin off; it sends pins and needles up the leg as far as the knee." The right palm can be easily tickled, but on the affected hand she cannot bear this stimulation; it evokes a strong reaction, gives a sensation "as if red-hot needles were being plunged into her," and starts a pain that spreads up the arm as high as the elbow. A wisp of cotton-wool rubbed over the pinnæ is appreciated more distinctly on the right, but tickles more and evokes a stronger reaction on the left. The same holds for the two sides of the chest. Rubbing a wisp of wool over the left nipple provokes an intense general reaction, but if her eyes are closed she has no idea where she has been stimulated.

She is most intolerant to scraping with the finger-nails on the whole of the left side of her body; it starts a widely spreading and very unpleasant sensation of burning.

Vibration.—She is unable to appreciate even the strongest vibrations of the fork anywhere on the left limbs; there is considerable loss of appreciation even over the left malar bone as compared with the right.

Sensibility to pain.—When the left hand is pricked she replies at once, "Oh, that is ten times worse than on the right; it sends a pain right up to my elbow." "The prick is not at all the same as on the right; on the left it goes all over my hand, while on the other side it stays in the one place." "It is horrible on the left; it is a dreadful burning pain." Every prick on the affected hand provokes an intense reaction and the patient is most reluctant to submit to it. There is apparently little or no persistence of the sensations evoked.

Similarly on the left side of the face, of the chest, and on the leg, pricking produces an intense reaction and more pain and discomfort than on the right side, and the pain spreads widely from the spot stimulated. She has usually little or no idea of the locality of the spot that is pricked.

On testing with the algesimeter it is found that the threshold for pain appears to be slightly raised on the affected side. The following figures

represent the lowest values that produced a sensation of pricking with the spring-algesimeter.

				R.	L.
First dorsal interspace	3	grm.	5	grm.	
Dorsum of middle-finger.. .. .	2	„	3	„	
Dorsum of forearm	3	„	3	„	
Front of chest	2	„	2	„	

Pressure-pain.—The application of the algometer produces a much "sorer" sensation on the left side than on the right, and provokes a much greater reaction. Further, the pain develops explosively on the affected side and spreads widely. The following figures represent the threshold-values on corresponding parts of the two sides.

				R.	L.
Palm	5	5½	4½	4	3½
First metacarpal bone	3½	3½	3½	2½	3 3½
Front of shin	3	3	8	4	5 5
Sole	4	4		3	3½

Thermal sensibility.—She has lost completely the appreciation of temperature on the right side, excepting perhaps on the face. The mean degrees evoke no sensation, but the extreme degrees produce pain and an excessive response which may be called indiscriminately hot or cold. Thus when a tube at 60° C. was applied to the palm she cried out, "Oh, I have a pain up my arm, it is as if you were pouring boiling water over my arm; it's like a wheel running over my arm." And when a tube containing ice was applied immediately afterwards she reacted similarly and said, "It is just the same, but not so bad; it is as if you had turned a fountain of boiling water on at my shoulder." On the palm, temperature below 25° C. and above 50° C. produced this discomfort; those necessary to do so on other parts of the affected side varied slightly from these degrees. The pain did not usually develop till the tube had remained for some time in contact with the skin.

During these tests it was observed that while high or low temperatures produced pain and discomfort, mild warmth frequently evoked a reaction of pleasure. This aspect of temperature was consequently tested, employing larger tubes in order to cover a greater surface of skin. It was found that though the stimuli could not be recognized as thermal, temperatures between 38° C. and 43° C. were positively pleasant to the affected side, much more so than to the normal side, and that they could evoke a very definite reaction of pleasure. Thus, when she was asked to describe the sensations produced by 40° C. applied successively to the two sides of her chest she said, "Oh, that is very nice on the left; it is comforting, I like it there. It feels warmer on the right side, but it is not nearly so soothing, or so pleasant." 43° C. was "very pleasant" to the left palm, and she seemed reluctant to allow the tube to be taken away; while when 41° C. was placed on the sole she exclaimed "Oh, that's nice: I would like it there all day." She occasionally called these pleasurable temperatures warm, but careful testing makes it improbable that they evoked any thermal sensation.

Thus, though there is complete abolition of thermal sensibility, high and low degrees of temperature produce on the affected side excessive discomfort and an exaggerated reaction, and mild warmth is more pleasant and evokes pleasurable sensations on this side.

Sense of position.—There is total loss of knowledge of the position of the left arm and leg; she has not the slightest idea where these limbs lie.

Appreciation of passive movement is also completely lost in the left arm and leg; she does not recognize that anything is happening even on maximal movements of the fingers or hand.

Localization of tactile stimuli cannot be tested owing to the great loss of touch on the affected side, but she seems to have a very imperfect knowledge of the situation of painful stimuli.

Appreciation of weight is also completely lost, whether tested on the supported or unsupported hand. She cannot recognize any difference between an empty case weighing 5 grm. and the same case containing 500 grm.

Recognition of form is also completely abolished in the left hand.

Owing to the extreme tactile insensibility the *compass-test* could not be carried out, and it was impossible to test *size, shape, or texture*.

CASE 11.—*An instance of the thalamic syndrome where states of emotion were manifested on the affected half of the body by increased involuntary movements and disagreeable sensations.*

Mrs. A. R., aged 52, has been under the care of one of us (H. H.) for the past four years. In 1902 she began to notice tremor of the right arm and the right leg. Three months later, whilst talking at the telephone, she suddenly fell; she found she could not move the right limbs, but does not think she lost consciousness. She remained in bed a week. The loss of power passed off rapidly, but she then discovered she had lost control of the limbs of the right side, probably in consequence of the loss of sensation; for from that time she found she was not aware of the position of the right limbs when she could not see them, as in the dark or when her leg was underneath the table. For a day or two after the stroke she had no "feeling" in the affected half of the body, but sensation returned rapidly and she then began to suffer from pains throughout this side. The involuntary movements which had existed before the stroke returned more vigorously with the recovery of power. Speech was never affected, there was no diplopia, and the functions of the sphincters were not disturbed.

CONDITION IN 1910.

She is a healthy-looking, unusually cultivated and intelligent woman. The circulatory system is unaffected, the vessels are not thickened, arterial tension is not raised, and the urine does not contain sugar or albumen.

Special senses.—Vision, smell, and taste are unaffected, but hearing is slightly diminished on the right side.

Ordinary sounds, such as the note of a tuning-fork or the sound of a bell,

produce no abnormal effect, but all music that is capable of stirring her emotions excites the unpleasant sensations in the right half of the body. She has always been musical and, up to the time of the stroke, enjoyed good music intensely; but since the attack all such music excites the uncomfortable sensations in the right half of the body and exaggerates the involuntary movements. The singing of a so-called comic song leaves her cold, but serious music is so intolerable, owing to the sensations it produces throughout the right side of her body, that she is obliged to leave the room (*vide* p. 135).

Cranial nerves.—The functions of all the cranial nerves are unaffected; the pupils are equal and react well to light and on accommodation.

Motor system.—The left limbs are normal. The muscles of the right limbs are equal in size to those of the left. The tone of the leg is slightly greater on the affected side, but there are no contractures. All movements are possible, and their range is good, excepting those of the toes. The strength of movements of the right lower extremity against resistance is somewhat less than of the left, dorsiflexion of the foot being especially feeble. The grasp of the right hand is not quite so strong as that of the left, but there is no paralysis or contracture of the limb. Constant involuntary movements of the different segments of the right limbs are present, due apparently to alternate contractions and relaxations of muscles and their antagonists. This tremor, whilst it affects any one segment of the limb, seems to be fairly regular in rate and amplitude, but it frequently spreads from one part to another, or may affect several segments at the same time. It is greatly increased by voluntary movement or by anything that leaves a segment of the limb unsupported. She is unable to control this tremor voluntarily.

Reflexes.—The tendon-jerks are brisker on the right side than on the left, but ankle-clonus is not obtained. The plantar reflex on the left foot is of the flexor type; there is little doubt but the reflex from the right sole is also normal, but any attempt to elicit it from this foot produces so violent a movement of withdrawal of the whole of the leg, and evokes so much discomfort that it is difficult to investigate.

Spontaneous sensations.—She complains of many different abnormal sensations in the right half of the body. The right hand seems swollen and cramped, "as if I had been riding a pulling horse," and the toes of the right foot feel as if they were curled up underneath. "The foot seems round and not flat on the ground." As a rule there is no spontaneous pain in the affected limbs as long as she lies quietly in bed, but directly she is up and about a dull aching pain sets in over the whole of the right half of the body. She also complains of a "cold stinging feeling" in the right hand, and not infrequently in the right foot. She objects intensely to anyone sitting to her right side, for she then begins to suffer from the same disagreeable sensations in this half of her body that are evoked by contact. When one of us placed himself to her right without touching her she complained of a "soreness all down the side, as if you were pulling a dressing from a wound." This ceased entirely when the observer moved to her left. This phenomenon seems to be not uncommon in this class of cases and we have met with it in two other instances.

Tactile sensibility.—She recognizes cotton-wool contacts on both hairless and hair-clad parts of both halves of the body, but says there is a considerable difference between the sensations evoked on the two sides: "On the left it is quite distinct, but on the right it is as if you touched me more lightly." A threshold is obtainable on the right hand with a hair of 70 grm./mm.², whilst on the left she had no difficulty in appreciating every contact with a hair of 14 grm./mm.² On the affected side, however, the records of serial contacts tend to be confused by the persistence of sensation.

Roughness.—As measured by Graham-Brown's instrument, the same amount of protrusion is required to produce a sensation of roughness on the two halves of the body, but when the same stimulus is compared over similar parts she says it is "harder and rougher on the left side, but more uncomfortable and scratching on the right side."

Tickling and scraping.—When a wisp of cotton-wool is lightly brushed across the left ear she smiles and says it is "quite pleasant," but when the right ear is treated in the same manner she withdraws and raises her hand to brush the stimulus away, saying it produces a "harsh and very unpleasant feeling which seems to open up the soreness of the side." When the left sole is stroked with the pulp of the fingers she smiles and does not withdraw her foot, but on the right even the slightest touch produces an intense reaction and she complains that the sensation is extremely unpleasant.

Vibration is appreciated on both halves of the body, but is shortened, and the fork appears to be beating more slowly on the affected limbs.

Sensibility to pain.—Pricks are "not so distinct" on the right as on the left half of the body, and the threshold is slightly raised; but a much greater reaction is evoked from the whole of the affected than from the normal side. A measured prick of the same strength "is not so sharp, but is far more unpleasant on the right side than on the left."

Painful pressure.—The reaction to the painful aspect of pressure is so intense on the right side that it is scarcely possible to measure sensibility to this stimulus. Thus, on the normal palm 5 kg. of pressure are necessary to evoke discomfort, whilst on the affected hand even half a kilogramme produces an intolerable sensation.

Thermal sensibility.—There is no defect of sensibility to temperature, and the thresholds for heat and cold are identical on the two sides. Moreover, there is no exaggerated response to extremes of heat and cold on the affected side.

Sense of position is gravely defective in the right limbs; she fails to describe or imitate correctly any position into which the right arm or leg may be placed.

Appreciation of passive movements is equally defective. She can, however recognize a passive movement and its direction if the range is sufficiently great, but no movement of the upper limb is appreciated until it has reached at least five times that necessary on the normal side.

		R.				L.			
Index-finger	Flexion	22		25 27		4 5		4	
	Extension	20	20		25	3 3		3	
Elbow	Flexion	17 16		20		3		2 2	
	Extension	12 15		15		2	3 2		

Localization.—Almost as good results were obtained on the right as on the normal half of the body with the usual tests, but she is somewhat slower, and herself recognizes that she was less certain on the affected side.

Compasses.—Sensibility to this test is considerably affected on the right half of the body; for instance, on the hand a record with the points 6 cm. apart is defective, while 1.5 cm. gives a perfect reading on the left palm. She is, however, able to appreciate the two points when applied successively. This defect cannot be due to loss of tactile sensibility, for in two long series of observations she made the same number of errors with the blunt-pointed compasses as when sharp points, which pricked her, were employed.

Appreciation of size is seriously defective, but she is able to appreciate the relative size of two objects when they differ by something over twice the amount necessary on the normal side.

Appreciation of shape and form.—Although she made no mistakes with our test-objects on the normal side, she was frequently wrong on the affected hand; she says, "I have an idea of the shape, but I am not certain." She can recognize many common objects, such as a pencil, scissors, a watch, a knife and a key.

CASE 12.—An instance of the thalamic syndrome where all loud sounds produced great distress and much increased the involuntary movements on the affected side.

Frederick W., aged 65, was admitted into the London Hospital under the care of one of us (H. H.) in May, 1911. He was an engine-fitter, and was perfectly well until April 15, 1910. On that day, as he knelt down to tie some heavy objects on to his barrow, he became dizzy and lost consciousness. He remained unconscious for two or three days with complete left hemiplegia. Movement of the left arm and leg gradually returned; about a month after the stroke the involuntary movements appeared and from this time increased steadily in violence. Since he regained consciousness he has constantly complained that noises were peculiarly unpleasant to him, and at the same time he found that he could not hear so well with the left ear; this seems to have followed directly on the stroke. Vision was not affected and there was no diplopia at any time. There was no disturbance of smell or taste.

The pains which are now so prominent a feature of his case came on about three or four weeks after the stroke, and have since then increased in severity.

CONDITION IN MAY, 1911.

He is a worn-looking old man with thickened vessels and somewhat raised arterial tension. Otherwise there is no visceral disease. The urine contains no albumen or sugar. He is fairly intelligent, and as long as he is not exposed to noise is quiet and attentive.

There is no aphasia or apraxia, but when he is excited he shows a curious difficulty in expressing what he wants to say. He stammers and can scarcely utter a word; at the same time the left arm is thrown into violent movement. If he is allowed to remain quiet for a time these movements subside, and he can then enunciate all his words perfectly.

Special senses.—Smell, taste and vision are unaffected. On the other hand, hearing shows the following changes: If a tuning-fork is held near either ear, whilst he is in an absolutely quiet room, he listens for a few seconds calmly and then becomes more and more agitated; his face shows obvious signs of discomfort and the involuntary movements of the affected arm become greatly increased, or they may be started by the sound of the fork. It is difficult to be certain that the tuning-fork is a more potent cause of discomfort and exaggerated movement of the affected arm when placed near the one or the other ear, but our impression after several examinations is that it is easier to produce these effects from the left ear. Moreover, he is certain that he dislikes the fork more when it is approached to the left ear than to the right. Music, of which he used to be unusually fond, is now intensely disagreeable; even favourite tunes "now work me up till I can't bear them," and excite the involuntary movements to great violence and amplitude. On the day he travelled to London the noise of the railway was so intolerable to him that he attempted to throw himself out of the train. No musical sounds are now capable of giving him pleasure.

On examination it is found that whispering and the watch are equally well heard in the two ears, and there is no gross difference between the appreciation of the various tuning-forks. The right meatus is narrow and the left more so; the membranes are slightly grey and thickened, but there is otherwise nothing abnormal. Thus, though there was a history of "deafness" after the stroke, no loss of hearing can be now demonstrated in the left ear.

Cranial nerves.—The ocular movements are unaffected and the pupils react well. The right corneal reflex is brisk, but the left is abolished. The masseters contract equally. When the patient is at rest the left half of the face is somewhat more contracted than the right, and the nasolabial fold is deepened; the two sides move, however, equally in strong voluntary movement, but in speech irregular overaction of the whole of the left half of the face occurs, including even the muscles of the forehead. These irregular movements are particularly liable to appear under all conditions that provoke or exaggerate those of the left arm. The movements of the palate and tongue are unaffected, but occasionally spontaneous movements are seen in the left half of the tongue.

Motor system.—The right limbs are unaffected. The muscles of the left limbs are not wasted, their tone is normal and there is no rigidity or contracture. The strength of the arm is excellent; any apparent weakness is due to the gross ataxia. As he lies quietly in bed the left hand and forearm are usually in constant irregular movement; the movements resemble those of a child that is fidgety, or of a man who is ill at ease when speaking. But, when he is excited by noises or emotional causes, they increase and become almost flail-like; the arm swings around, dashes against his bed or his body with astonishing violence, and the leg is similarly agitated, though the amplitude of its movements is less. These movements disappear in sleep, and when he wakes his limbs are at rest. In addition, all voluntary movements of these limbs are extremely ataxic. His gait varies with the vehemence of the involuntary movements of the left leg; when they are slight he can walk without difficulty in spite of the obvious ataxia of the leg, but when the movements are excited they often become so violent as to prevent him walking.

Reflexes.—All deep reflexes are brisk but equal on the two sides. Both plantars give flexor responses, and the abdominal reflexes are equal on the two sides.

Spontaneous sensations.—He complains of constant pains over the whole of the left half of the body, sometimes stationary in the neighbourhood of the great joints, sometimes shooting through a limb or over the whole side. They are liable to be evoked by peripheral stimuli that cause discomfort. He also complains of a "numbness" down the left half of the body, "as if it had been hurt and bandaged up." The left side and this half of the face seem to him to be puffed and swollen, and there is a "cold feeling" round the left eye. If he lies on the left side it seems as if he were "on a hard lump."

Tactile sensibility.—There is complete loss of sensibility to contacts with cotton-wool on the left arm, left leg and this half of the trunk, but he occasionally responds to wool rubbed over the left ear and forehead. Pressure-touch is also gravely diminished.

Roughness.—He appreciates roughness, as tested with Graham-Brown's instrument, within normal limits on the right half of the body, but even when the protrusion is five times this amount he fails to recognize the scraping of the instrument on the left side. Under these conditions he merely says, "Something is happening to me, but I don't know if you are doing anything."

Tickling and scraping.—Although cotton-wool may not be appreciated over the left lower limb, a wisp repeatedly rubbed over the sole produces a sensation of painful "tingling all up the leg." When the pulps of the fingers are gently drawn over the right sole he smiles but remains still, but when the same stimulus is applied to the left sole his face shows obvious discomfort and he says, "You are tickling me, but it does not seem any place in particular; it is a crawling feeling which affects me all up the side." When the left sole is scraped with the finger-nails he shows signs of distress and says, "I don't know what you are doing, but it affects me all up the side." Both tickling and scraping excite and exaggerate the involuntary movements.

Vibration.—The appreciation of vibration is totally lost on the left limbs and on the left half of the trunk, and no unpleasant sensations are provoked by the application of the strongly vibrating fork.

Sensibility to pain.—He generally fails to appreciate moderate single pricks on the left upper limb, but when pricked more firmly, or several times in succession, he reacts vigorously, describes the sensation as "something burning," or "a sharp, fiery prick," and says it is much more painful than on the opposite side. On the chest he replies more frequently to a single light prick, and there is extreme over-reaction to the point of a pin when, being dragged from right to left, it crosses the middle line. The threshold to prick is evidently raised on the left side of the face and on the left leg, but a series of pricks produce the same uncomfortable burning sensations as on the affected arm. Pricks on the left side are also "more uncomfortable because they affect me all over." He has no idea of the situation of the pricks; whether on the elbow or on the back of the hand, they are equally referred to the palm. He also confuses a series of pricks on the shin with the effect produced by tickling the left sole with the pulp of the fingers; not only does he confuse the locality of the sensation, but he has no idea of the different nature of the stimuli.

Measurements with the algesimeter also show that the threshold is greatly raised on the whole left half of the body, excepting the left sole. Here the same strength of stimulus evokes pain as on the right sole, but the reaction is invariably greater.

Pressure-pain.—The pressure necessary to evoke pain is uniformly higher over the left than on the normal half of the body, but the pain evoked is excessive. Thus, over the normal sole he complained of pain with a pressure of 3 kg., and at 5 kg. the signs of distress were considerable; but on the left sole no pain was produced until the pressure had reached at least 5 kg., and yet he complained that this stimulus was much more uncomfortable on the left than on the right sole.

Thermal sensibility.—All appreciation of temperature is abolished on the left half of the body. Ice produces an uncomfortable sensation over the affected parts, which he describes "as if something pricked me and made me jump," and the reaction is greater than from the normal side. No temperature between 10° C. and 50° C. produces any reaction.

Sense of position and of passive movement.—He is totally unable to recognize the posture or passive movements of the left limbs, and makes no attempt to say in what direction they are moved.

Localization.—He has lost the power of recognizing the locality of all stimuli, including prick and painful pressure. He can generally recognize in which limb pain is evoked, but has no idea what part of the limb the stimulus affects.

Compasses cannot be tested owing to the gross loss of tactile sensibility.

Appreciation of weight.—He is unable to appreciate weight in the left hand and cannot even recognize the difference between 30 and 700 grm., whether the hand is supported or not.

The power of *appreciating form* is also abolished in the left hand.

Visceral sensibility.—There is no doubt that the left testicle is less sensitive to pressure than the right, but when pain is evoked by squeezing it strongly he says, "It feels sharpest on the right, but I would rather you did not squeeze the left."

CASE 13.—*An instance of the thalamic syndrome where the loss of sensation was extreme and the thresholds for all painful stimuli, including the pressure-algometer, were greatly raised.*

Thomas G., aged 43, was admitted to the National Hospital, under the care of Dr. Turner, in August, 1910. On May 4, 1907, whilst at work, "a numbness" appeared in the right foot and gradually spread up the right half of the body. During the next half-hour he found his right arm and leg became weak and his speech was affected. He was taken to a hospital and remained there in bed for nearly seven weeks. Speech returned rapidly, and the loss of power in the limbs gradually passed off. About eight months after this stroke the right limbs began to shake: the involuntary movements have always been worse in the arm. The stroke produced immediate loss of sensation in the right half of the body; but the pains and the tingling did not set in till some months later. The special senses were not affected by the stroke.

CONDITION IN SEPTEMBER, 1910.

He is thin and prematurely aged; his radial vessels are thickened and tortuous, but the pulse-tension is not raised. Urine is of low specific gravity and contains no albumen or sugar.

He is illiterate, but answers well to direct tests; although he becomes tired easily, his memory is fair. There is now no evidence of affection of speech, or of apraxia.

Special senses.—Smell, taste, hearing and vision are unaffected.

Cranial nerves.—The functions of all the cranial nerves are normal, except that the right corneal reflex is much diminished.

Motor system.—The left limbs are unaffected. There is a general increase of tone in the muscles of the right limbs and slight rigidity, but the range of movement is not restricted and there are no contractures. The strength of all movements is remarkably good, and there is little difference between that of the limbs of the two sides; even isolated movements of the right fingers can be easily performed, but more slowly and awkwardly than on the left side. All movements of the right limbs are, however, very ataxic and accompanied by a definite intention-tremor.

But in addition the limbs of the right side are the site of involuntary movements, which usually take the form of a tremor that is irregular in both amplitude and rate. This tremor is most evident in the distal segments of the limbs, but is present even at the shoulder and hip. Occasionally, more irregular movements, which can be described as choreiform, also occur; these

are increased on any attempt at voluntary movement. He walks fairly well but holds the right leg rigid, and its movements are poorly directed and co-ordinated.

Reflexes.—All the tendon-jerks are increased on the right side as compared with the left, and ankle-clonus can be obtained, but both plantar reflexes give flexor responses. The abdominal and cremasteric reflexes are obtained on the left side but abolished on the right.

Spontaneous sensations.—He complains of pains throughout the whole of the right half of the body, which are not only constant but are subject to intense exacerbations which last from three to four hours. These are particularly severe in the face and at the back of the eye. He also suffers from "pins and needles" in the right hand and the right foot, which arise without obvious cause. The right arm seems "numb" as high as the elbow, and the right leg up to the knee.

Tactile sensibility.—Over the whole of the right half of the body and the right limbs there is considerable diminution of tactile sensibility. Even when cotton-wool is rubbed across the part his answers are irregular and he often fails entirely to appreciate the stimulus. Sensibility to pressure-touch is also much diminished.

Tickling and scraping.—On tickling the sole of the left foot a strong reaction is obtained, but the sensation is not unpleasant; but from the right sole the sensation is distinctly unpleasant, "as if your nails were digging into my flesh," and the movements which constitute the reaction are more extensive and violent than those which occur on the normal side. There is a similar difference on gently tickling the two palms. If these parts are scraped the difference is even more pronounced.

Vibration.—He cannot appreciate vibration on the upper limb, and the sensation produced by the tuning-fork is greatly diminished on the right half of the chest and the right leg and foot. No unpleasant sensations are evoked by this stimulus.

Sensibility to pain.—Sensibility to prick is greatly diminished on the whole of the right half of the body; on the upper extremity he fails to appreciate many strong pricks. While 2 gm., as measured with the algometer, evoked a sensation of pricking on the left hand, 22 gm. was the minimum pressure that could evoke pain on the right. Moreover, he always asserts that a pin pricks him more, and is more painful, on normal than abnormal parts, but at the same time the reaction evoked is considerably greater from the abnormal side. The unpleasant sensations spread widely on the affected parts. On the leg, however, where the loss of sensation is less, the pain and discomfort, as well as the reaction, are greater on the abnormal side.

Pressure-pain.—The readings of the pressure-algometer are higher on the right half of the body than on the left, except on the sole of the foot; here half the pressure required on the left side produces pain on the right, and he objects more strongly to it.

Thermal sensibility.—On the whole of the left half of the body, except the

face, sensibility to temperature is completely abolished. Ice, and water at 60°C ., cannot be distinguished, but both evoke painful or more uncomfortable sensations than on the normal half of the body.

Sense of position and the *appreciation of passive movement* are completely abolished in the right limbs; thus even a movement of 90° at the right elbow fails entirely to produce any sensation.

Localization, the *compasses* and the *appreciation of size and shape* cannot be tested owing to the gross loss of sensibility.

He fails to recognize any of the ordinary test-objects for *form*; and on testing for the appreciation of *weight* it is found that he cannot recognize even 200 gm. placed in the right hand.

Visceral sensibility.—On compressing the testicles gently, not only does he say that it is more painful on the abnormal side (right), but the expression of discomfort and the reaction are excessive compared with that from the left.

CASE 14.—*To illustrate the consequences of removing a small portion of the cortex in the region corresponding to the motor centre for the arm and hand.*

Reginald H. This is the patient from whom Sir Victor Horsley removed a portion of the precentral gyrus in March, 1908, at the age of 14. He formed the basis of the Linacre Lecture [13] in 1909. Owing to the kindness of Sir Victor Horsley, to whom we are much indebted, we have been able to examine this patient from time to time between April, 1908, and the present date (1911). Our most complete observations were made between October, 1909, and October, 1910.

For the nature of the operation and the structure of the tissue removed we must refer to Sir Victor Horsley's account; but, roughly speaking, the part removed contained the foci from which movements of the left upper limb could be excited by electrical stimulation at the time of the operation. It consisted of a portion of the precentral gyrus, $4\frac{1}{2}$ cm. in vertical extent, with its middle point somewhat above the genu of the fissure of Rolando. In this account we shall summarize his condition subsequent to October, 1909, for since that date the signs and symptoms have shown no material change.

He is an extremely intelligent youth, a good witness, and willingly submits to prolonged examination.

Special senses.—Smell, taste, hearing and vision are unaffected.

Cranial nerves.—The functions of all the cranial nerves are carried out normally; the movements of the face are symmetrical and the tongue is protruded straight.

Motor system.—The bulk of the muscles of the left forearm and hand is slightly less than that of the right, and their tone is distinctly increased. The limb is rigid, but there are no organic contractures. Voluntary power is considerably diminished in the left arm, more particularly in the fingers, but at the shoulder and elbow the movements are of fair strength and good range. He walks normally and can even play lawn-tennis; there is no difference between the strength or the tone of the muscles of the lower extremities.

Reflexes.—The arm-jerks are exaggerated on the left side, but the knee- and ankle-jerks are equal, and both plantar reflexes give flexor responses.

Spontaneous sensations.—He complains of no spontaneous sensations, except that when the arm is cold it "feels numb."

	Normal hand (R.)	Affected hand (L.)
21 grm./mm ²	O	
21 grm./mm ²		O O
23 grm./mm ²		O O
35 grm./mm ²		::
70 grm./mm ²		
100 grm./mm ²		O
23 grm./mm ²		O O O O
35 grm./mm ²		: O
70 grm./mm ²		
23 grm./mm ²		O O O O
21 grm./mm ²		
21 grm./mm ²		
23 grm./mm ²		
35 grm./mm ²		
70 grm./mm ²		
100 grm./mm ²		

To illustrate a set of records obtained in Case 14 when the hands were stimulated with von Frey's hairs of different strengths. On the affected side a threshold could be obtained, but the records were disturbed by hallucinations and other irregularities. His answers from the normal hand were remarkably constant.

Tactile sensibility.—On the normal hand and on both feet a perfect series of answers can be obtained with a hair of 21 grm./mm.²; but on the affected hand the answers are slower and less constant, the sensation of contact tends to persist after the removal of the stimulus, and hallucinations frequently disturb the records. It is possible, however, with care to obtain evidence of a definite threshold.

Roughness and vibration are appreciated equally on the two sides, and measurement gives the same threshold for both on the two upper extremities.

Tickling and scraping are equally appreciated on the two hands and arms.

Sensibility to pain.—Careful measurements with both the prick-algesimeter and the pressure-algometer fail to reveal any difference of threshold for pain on the two upper limbs, or elsewhere on the body. Further, the reaction of the two sides to painful stimuli is identical.

Thermal sensibility.—There is no demonstrable alteration of sensibility to temperature, and the thresholds for heat and cold are identical on the two hands; thus, on one occasion the neutral zone lay between 28°C. and 30°C. on both palms and the palmar aspects of the fingers. There is no abnormal reaction on either side to the extreme degrees of temperature.

Sense of position.—The power of recognizing the position in space of the left arm, and especially of its distal segments, is gravely defective. Thus, if it is placed in any position, when his eyes are closed, he has difficulty in finding the index-finger, and even if he succeeds in striking some other portion of the hand, such as the middle-finger, he cannot immediately discover the index-finger from its relative position. Examination with Horsley's plate demonstrates this defect very clearly. He visualizes strongly and obtains a clear mental picture of both hands. When his eyes are closed this mental picture of his normal hand alters with movement of any part of it; thus, if the index is flexed he sees the finger in its new position. But under the same conditions no amount of passive movement alters the mental picture of the left hand; consequently he refers any sensation evoked on the hand, after its situation has been altered, into its old position in space. For instance, he was asked to lay his hand on the table; after his eyes were closed the elbow was flexed passively to a right angle and when it had been supported in this position for some time various stimuli were applied to it. In his visual picture the hand still lay on the table, and, when asked to point with his sound index-finger to the spot stimulated, it was in this direction he first attempted to find it.

He has a perfect knowledge of the position of the various segments of the left lower limb.

Appreciation of passive movement is gravely affected at all joints of the left upper extremity below the elbow, but more particularly in the fingers of the left hand.

		Normal (R.)					Affected (L.)				
Index-finger	Flexion	2	2	2	2	$1\frac{1}{2}$	40+	50+	50+	30	50+
	Extension	2	2	3	$2\frac{1}{2}$	2	30+	40	60+	55	60
Elbow	Flexion	$1\frac{1}{2}$	$1\frac{1}{2}$	1	$1\frac{1}{2}$	$1\frac{1}{2}$	10	$7\frac{1}{2}$	8	6	$7\frac{1}{2}$
	Extension	2	2	1	$1\frac{1}{2}$	2	6	6	9	8	6

These numbers give the angles in degrees of the smallest movements which were appreciated; wherever the numbers bear a + the movement was appreciated, but not its direction.

Localization.—When he is asked to grope for the situation of a stimulated spot on the affected hand he can rarely find it on the first attempt, but he can describe without difficulty the position of the spot that is touched; it is obvious, therefore, that the errors he makes with the groping method are due to his want of knowledge of the position of the limb rather than to defective power of localization. This is confirmed by observations made with both the original and the modified Henri methods, for the results obtained by both are as accurate on the affected as on the normal hand.

Compasses.—The power of discriminating two points is very defective on

the left hand, but becomes steadily better as the limb is ascended. Thus on the normal palm a perfect reading can be obtained with the points 1.5 cm. apart, but in the left palm a threshold cannot be obtained even when they are separated to 6 cm.; on the normal forearm the record is perfect with the points separated to 5 cm., whilst on the left side a threshold cannot be obtained below 15 cm.; between the elbow and the shoulder the difference is considerably less, for although 6 cm. is required on the right side a perfect reading can be obtained on the left arm with the points 10 cm. apart. On the upper part of the chest the difference between the two sides is even smaller, and over the hypochondrium the thresholds are identical on the two sides. Step by step with this increased power of discrimination, the slowness and uncertainty of his replies steadily diminishes, until, when tested on the hypochondrium, they are as quick on the left half as on the right. No difference to this test can be found on the lower extremities, and the records obtained from the two sides are equally good.

		Normal (R.)		Affected (L.)		
Palm, 1.5 cm.	1.5 cm.	$\left\{ \frac{1}{2} \right $	II III I II II I	$\left\{ \frac{1}{2} \right $	II IOII IXXX XII OXX XX XI	
	6 "	$\left\{ \frac{1}{2} \right $	III I I II II I	$\left\{ \frac{1}{2} \right $	XXXI IXXXI I XXXI XXXXI X	
Forearm, 5 cm.	10 "	$\left\{ \frac{1}{2} \right $	III I II I II	$\left\{ \frac{1}{2} \right $	II I III IXIX I IIXI IXXXX	
	15 "	$\left\{ \frac{1}{2} \right $	II III II I I	$\left\{ \frac{1}{2} \right $	III III III I III III II	
	Arm above the elbow	6 cm.	$\left\{ \frac{1}{2} \right $	III II III I	7 "	$\left\{ \frac{1}{2} \right $
	10 "	$\left\{ \frac{1}{2} \right $	II III III II	10 "	$\left\{ \frac{1}{2} \right $	III III I II II IIXI II II

As soon as the points are applied successively, with only the fraction of a second between the moments at which the first and the second points touch the surface of the body, he recognizes the double nature of the stimulus without difficulty. This was well shown by a series of observations in which the compass-points were so applied that each fell on a different finger; when they were applied simultaneously, for instance to the index- and middle-fingers, he never recognized the double stimulus, or that he had been touched on two fingers; but as soon as a fraction of a second was allowed to elapse between the contact of the one point on the middle-finger and the other on the index, he at once recognized that he had been touched with two points, and that they had fallen on two fingers. This is true for all the fingers.

Appreciation of weight is gravely disturbed on the left hand, whether the limb is supported or unsupported; he cannot even recognize with certainty the addition or removal of weights, such as 100 grm., to or from a weight of 15 grm. resting on the palm.

The power of appreciating *size, shape, form in three dimensions, consistence and texture* is lost in the left hand, and he complains that the test-objects do not seem to have shape or form. On the normal hand his power of recognizing these tests is remarkably good.

CASE 15.—*To illustrate the effect upon sensation produced by removal of a portion of the cortex in the right parietal region.*

George M., aged 48, formerly a foreman on a railway, is at present an out-patient under the care of one of us (G. H.) at the National Hospital. In August, 1905, he was admitted to hospital under the care of the late Dr. Beevor with the symptoms of an intracranial tumour. In May of that year he first had an attack of left-sided convulsions, which began in the hand and later affected the leg and this side of his face; the convulsions were preceded by numbness of the hand. This seizure was followed by others which seemed to have been exactly similar, and to have recurred at diminishing intervals. He suffered from a little headache on the right side of his head, but did not vomit.

On admission to hospital slight optic neuritis was present in both eyes, but no other abnormal signs could be found except a slight diminution of sensation on the left hand and forearm, affecting chiefly the sense of position, with "astereognosis." The reflexes at that time were normal. As the optic neuritis increased, and some weakness of the left arm developed, he was operated on by Sir Victor Horsley on October 31, 1905, and a large gumma attached to the dura mater was removed, with a part of the subjacent brain tissue to the depth of 2 cm., from over the right inferior parietal lobe; it probably involved the lower half of the postcentral gyrus and a part of the supramarginal convolution, and at its inferior angle it extended frontalwards over the fissure of Rolando. The tissue removed was almost circular and measured 6 cm. in diameter. This description of the site of the operative lesion can be confirmed at the present time by careful measurements of the trephine opening in the skull.

For a time after the operation there was considerable weakness of the left arm, reaching complete paralysis in the hand, and much disturbance of sensation, especially of the sense of position, in this limb. There was also complete left hemianopsia. The paralysis and the sensory disturbances diminished considerably, and in the following description we shall summarize the observations made on his state between October, 1910, and the present time.

CONDITION IN 1910 TO 1911.

Since the operation he has suffered at rare intervals from slight left-sided epileptiform convulsions, for which he remains under treatment. In making the following observations we have been careful to avoid periods in which there was a risk of confusion from postepileptic phenomena.

He is an intelligent man, and is now actively engaged in selling newspapers. His memory and attention are good, and he submits willingly to protracted examination. Speech is not affected, and there is no apraxia. Smell, hearing, and taste are unaffected, and at present the visual fields are not contracted.

Cranial nerves.—The functions of the cranial nerves are unaffected, except that the volitional movements of the left angle of the mouth are a little slower and weaker than on the right, and that the tongue is protruded slightly to the left.

Motor system.—The right limbs are in every respect unaffected. There is a slight general wasting of the muscles of the left hand and forearm, but otherwise those of the two sides are equal in bulk. The tone of the muscles of the arm, and to a less extent of those of the leg, is increased, and the rigidity of the limbs offers a considerable resistance to passive movement; there is also a tendency to contractures, especially in the arm, but the range of voluntary movement is fair. The strength of all the arm-movements is diminished, but the leg is almost as strong as its fellow; the movements are awkward and slow, but not definitely ataxic. No involuntary movements occur. Gait is almost natural, but he drags the left foot when it is cold and numb.

Reflexes.—The left arm-jerks are exaggerated, and the left knee-jerk is a little brisker than the right. Ankle-clonus cannot be obtained, and both plantar reflexes give flexor responses.

Spontaneous sensations.—He complains of a numbness or "a sleepy feeling" in the left hand, especially in the fingers; here it is constant but varies in intensity. There is also some numbness of the left leg, chiefly over the foot. When he wakes at night he does not know the position of the left arm until he touches it or moves it about. He has no visual memory, and when he closes his eyes he sees no mental picture of either hand.

Tactile sensibility.—He cannot appreciate cotton-wool touches with certainty on the hairless parts of the left hand, and even on the hair-clad parts many stimuli evoke no response. This diminution of sensibility grows less towards the proximal portions of the limb, but he states that over the whole left upper extremity sensations of contact are "duller" than over similar parts of the right side. On the right hand a hair of 21 grm./mm.² is obviously above the threshold, and 23 grm./mm.² gives perfect readings; but on the left hand his answers are irregular and tend to be disturbed by hallucinations and persistence. Moreover, although he can appreciate 21 grm./mm.² on the affected hand, increasing the strength of the stimulus makes no constant improvement in the proportion of correct answers (*vide* p. 242).

Even the application of 32 grm. on a disc 3 mm.² could not evoke a perfect series of replies, although he was sensitive to the contact of the same instrument weighted with 2 grm. (*vide* p. 150). Thus it is obvious that in this case a tactile threshold cannot be obtained to measurable stimuli.

Roughness.—The threshold obtained with Graham-Brown's instrument is identical on the two hands, and there is no difference in the reactions evoked.

Tickling and scraping.—There is no difference in reaction from the two sides, but he says that cotton-wool rubbed across the hair-clad parts of the left hand tickles slightly less than on the right.

Vibration.—The tuning-fork is appreciated everywhere, but the sensation it evokes seems to him fainter on the affected than on the normal hand. Moreover, vibration can be appreciated on the right hand for several seconds after it no longer causes a sensation on the left.

Sensibility to pain.—He can appreciate the prick of a pin everywhere on the affected side of the body, but says, "It is not quite so sharp, and not so plain" as on the normal side. This want of "plainness" on the left hand and forearm is associated with an apparent slight raising of the threshold to measured pricks; this is more probably due to an affection of the discriminative rather than of the painful elements of the stimulus. There is no difference in the affective reactions from the two sides.

	Normal hand (R.)	Affected hand (L.)
21 grm./mm ²	○○	
23 grm./mm ²	○	
21 grm./mm ²		○○ ○○ ○○○
23 grm./mm ²		○○ ○○ ○○○ ○ ○
35 grm./mm ²		○○○ ○○○ ○○○ ○ ○
70 grm./mm ²		○ ○○○ ○ ○○○
100 grm./mm ²		○○ ○○ ○ ○○○
21 grm./mm ²		○ ○ ○○○○○ ○
23 grm./mm ²		○ ○ ○ ○
100 grm./mm ²		○

To show the results obtained when the affected hand is stimulated in a consecutive series with von Frey's hairs of different strength.

The readings of the pressure-algometer are identical on the two halves of the body.

Thermal sensibility.—To the ordinary clinical tests sensibility to heat and cold appears to be unaffected, and there is no difference in the reactions from any part of the two sides of the body. But more careful examination shows that the neutral zone is considerably enlarged on the left hand; thus on one occasion it lay between 29° C. and 31° C. on the normal hand, whilst on the affected hand all temperature between 27° C. and 36° C. seemed to be neither hot nor cold. Not only is the range of the neutral zone increased but the responses from the affected hand, compared with those from normal parts, are slow and irregular. Moreover, the power of comparing two thermal stimuli applied either together or in sequence to the left hand is diminished; for instance, although he can distinguish with certainty 40° C. and 50° C. on

the normal hand he is often unable to say which is the warmer to the left hand, although both appear to him to be warm.

Sense of position.—He is unable to recognize accurately the position in which his left hand and arm may be placed, and the sense of posture is also gravely defective in the left lower extremity.

The appreciation of passive movement.—Passive movement of the fingers and wrist cannot be appreciated even when they reach the extreme range possible without exerting tension on the muscles. He can recognize movements of large range at the elbow, but they must make an angle of at least 60° before he can recognize whether the joint is flexed and extended. Even at the shoulder a large range of movement is required for appreciation.

Localization.—When examined by naming, or by our modified Henri method, localization was found to be seriously affected on the left upper limb: out of fifty-three contacts on the left hand, twelve only were correctly placed, while on the normal hand he made no error in forty-five tests. This defect is equally evident when pricks are substituted for tactile contacts, and consequently it cannot be due to the disturbance of tactile sensibility (*vide* p. 163).

Compasses.—The power of recognizing the two points in this test is completely abolished on the left hand and forearm, whether they are applied simultaneously or successively. Moreover, the records are equally bad whether we use the ordinary blunt points or replace them by needles, so that every contact produces a prick.

Thus, on the dorsum of the right forearm a perfect reading can be obtained with the points separated to 4 cm., while on the affected forearm he fails to discriminate them when 20 cm. apart, even when they are applied with an appreciable interval between the two contacts.

Appreciation of weight.—The power of appreciating weight, even on the normal hand, is not acute. He can recognize the difference between 60 and 100 gm., but he is not uniformly correct with 120 and 200 gm., when these weights are applied successively to the normal hand. But in spite of the comparatively high threshold on the normal hand, the difference between the two hands to this test is very striking; for instance, when 30 gm. was placed on the fully supported left hand he recognized the contact, but not that the object had any weight, and even when 600 gm. were added to it and then removed he simply said: "You have moved the thing in my hand," and did not know that the weight had changed. When 60 gm. was placed in the normal hand and he was asked to compare it with the same weight in the affected hand by weighing with the unsupported hand, he said: "There is a weight in the right hand only."

Appreciation of size, shape, form and consistence.—All these faculties are entirely abolished on the left side. Moreover, he insists that in every case he can "feel" the test-objects placed in his hand, but he "has no idea" of their size, their shape, their form, or their consistence.

Visceral sensibility, as tested by pressure on the testicles and examination of the sensibility of the glans penis, is unaffected.

CASE 16.—*To illustrate the sensory changes found twenty-three years after an injury to the left cerebral hemisphere.*

Arthur William I., aged 42, is an out-patient under the care of one of us (G. H.) at the National Hospital. He was an officer in the merchant service. In April, 1887, he fell down the hatchway of a ship, injuring his head, and lay unconscious for three weeks. When he regained consciousness he was in a hospital in San Francisco; his right limbs were paralysed and he was unable to speak. During the five months he remained in hospital he regained some power in the right limbs. On the voyage home to England he began to suffer with convulsive attacks which affected the right hand and the right side of his face. He was admitted to the National Hospital under the care of Dr. Ramskill in November, 1888. There was then slight weakness of the right side of his face and considerable hemiplegic paresis and rigidity of the right limbs, with contractures of the fingers of the right hand. The right knee-jerk was brisker than the left, and right ankle-clonus was obtained. While in hospital he had several localized fits, which began either in the right thumb or in the fingers of the right hand; in several the convulsions were limited to the hand, but in others the right side of the face was also affected.

On April 2, 1889, Sir Victor Horsley operated and found a fracture of the skull which ran from before backwards across the fissure of Rolando. A large portion of the skull was removed, first over the region of the motor centres for the thumb and fingers, and then upwards to within $2\frac{1}{2}$ cm. of the middle line. The dura mater was adherent to the cortex and a subdural cyst was found at the posterior part of the opening. After the cortical vessels had been ligatured a portion of the damaged cortex, about 5 cm. in diameter, was removed; this included, as far as could be determined, the centres for the fingers and thumb.

CONDITION IN 1910.

He still suffers, at rare intervals, from local fits in the right hand, which occasionally spread more widely. Our observations were made for the most part in 1910, and we shall summarize in this account his condition towards the end of that year. There is at present no aphasia or apraxia; he is educated, fairly intelligent, and spends much of his time in playing chess matches.

Special senses.—Smell, taste, hearing and visual acuity are normal and the visual fields are not restricted.

Cranial nerves.—There is slight weakness of the right side of the face in voluntary movement, and the tongue deviates slightly to the right, but the functions of the cranial nerves are otherwise normal.

Motor system.—The right arm is smaller than the left and its muscles are firm and rigid; the wrist and fingers are held in a permanently flexed position, and contractures limit the range of passive movements at all joints. There is no power of movement of the fingers and hand, except that the fingers can be slightly flexed as a whole. Pronation and supination are impossible, and flexion and extension of the elbow are restricted and feeble; he can carry out

all the movements, except rotation, of the right shoulder, but they are feeble and he cannot bring the arm into a horizontal position. Voluntary movements of the right foot are also lost, but those of the knee and hip are fair in range and power. There is considerable rigidity of the whole limb, but no contracture except of the calf-muscles. He walks with a typical hemiplegic gait; the right leg is advanced by circumduction and he tends to drag the foot.

Reflexes.—All the deep reflexes are exaggerated on the right side and ankle-clonus can be obtained; the right plantar reflex gives an extensor response, and the abdominal reflex is much diminished on this side.

Spontaneous sensations.—He is not a good subject for introspection, but he says he thinks that the right arm and leg "go to sleep more easily than the left"; when he wakes up at night he is unable to find his right hand until he has groped for it. He has never experienced pain or tingling in the affected side.

Tactile sensibility.—When a wisp of cotton-wool is rubbed across the affected hand he appreciates most of the contacts, even on the palm, but he says that "the feeling is weaker" on the right than on the left, and that "it seems plainer" on the normal hand. There is no similar difference between the two lower limbs, where he appreciates contacts as constantly on the right as on the left. He has a high threshold to von Frey's hairs on the normal hand, but on the affected side no threshold can be obtained even to 100 gm./mm.² To the weight-æsthesiometer he gives a perfect series of answers on the left hand with a pressure of 2 gm., but on the affected a threshold cannot be obtained even with a pressure of 32 gm., although he responds to 2 gm. Moreover, increasing the strength of the stimulus makes no appreciable difference in the proportion of right answers; in fact, a better reading was obtained with 2 gm. than subsequently with 32 gm. With von Frey's hairs there is a great tendency to persistence and hallucinations, but this is much less evident during testing with the weight-æsthesiometer.

Roughness.—With Graham-Brown's instrument the same threshold is obtained on the two hands.

Vibration is everywhere appreciated, but on the right hand he said "it felt weaker" than on the left, and the period during which it can be appreciated is considerably shortened.

Tickling and scraping.—To tickling and scraping there is no difference between the palms, or the soles of the two feet.

Sensibility to pain.—When repeatedly pricked in any one area with a pin he says "it is stronger on the left side than on the right, but it does not hurt me more." Occasionally, too, he finds the prick "sharper" on the left hand. There is, however, no difference in thresholds on the two sides to measured prick or to pressure-pain.

Thermal sensibility.—The paralysed hand is usually blue and cold and is, therefore, unsuitable for the finer testing of thermal sensibility; but in spite of this he is able to recognize cold up to 15° C. and heat from 45° C. upwards. More satisfactory observations can be obtained from the arm above the elbow.

On the normal side the neutral zone lies between 27° C. and 32° C., whereas on the affected side it extends from 25° C. to 38° C. He complains that he can "feel warmth and coldness quicker on the left side than on the right" and adds, "I have to wait a minute to be sure on the bad side."

Sense of position.—The power of recognizing the sense of position of the right upper extremity is lost; he has no idea where it lies in space. There is also considerable loss in the right lower extremity, especially below the knee.

Appreciation of passive movement is also lost in the right fingers and wrist and is much diminished at the elbow; here a movement through an angle of even 60° was occasionally not appreciated, and the smallest movement he was able to recognize exceeded 40° . At the normal elbow he is always able to recognize a movement of 3° , and not infrequently indicates correctly the direction of a movement that does not exceed 2° .

Localization is remarkably accurate on the normal hand but is gravely affected on the right. When tested by the modified Henri method, he says to every contact; that he can feel it but has no idea where it is.

Compasses.—Readings on the dorsum of the hand and on the forearm showed that the power of discriminating two points is completely lost on the affected side, whether the two contacts are made simultaneously or successively.

Appreciation of weight.—He is completely unable to recognize the difference between two weights in the supported or unsupported hand; thus if equal weights are placed in the two hands he is conscious of the weight on his left palm, but does not recognize that the object on his right has any weight. Even when 500 gm. are placed in his affected hand he recognizes that something is in contact with it, but does not appreciate that it is a weight.

The *appreciation of size, shape, form in three dimensions*, and the recognition of familiar objects, are abolished in the right hand, although to all these tests he is accurate on the normal side.

CASE 17.—*To illustrate the application of our methods to a patient with sensory aphasia due to the removal of a portion of the cortex in the left parietal region.*

Edmund M., now aged 46, is at present an out-patient under the care of one of us (G. H.), at the National Hospital. He was admitted to the hospital under the care of Sir William Gowers in May, 1904, complaining of headache, vomiting, fits, weakness of the right arm, and difficulty of speech. These symptoms began eleven months before admission. In most of the fits he lost consciousness without local convulsions, but during the few weeks previous to admission he had had seizures which began with twitching of the right fingers; after these slighter attacks speech was particularly affected. Several of these occurred when he was in hospital, but convulsions were not observed in any of them.

At that time he showed distinct signs of sensory aphasia; the right upper

extremity was weak, but though he dragged the right foot no actual loss of motor power could be demonstrated in the right leg. The deep reflexes were brisker on the right than on the left half of the body, the plantar reflexes gave flexor responses, and ankle-clonus could not be obtained. He complained of numbness in the right hand, and on examination tactile sensibility was found to be slightly defective over the right arm and leg; the power of appreciating the position of right limbs was also disturbed and touches were badly localized. He was able to recognize objects placed in his right hand. Smell and taste were unaffected, hearing was poor in both ears, but bone conduction was better than aerial. Vision was fair ($\frac{6}{15}$ in both eyes), but there was slight peripheral contraction of the right halves of the visual fields. There was intense optic neuritis in both eyes. On June 21, 1904, a large gumma was removed by Sir Victor Horsley from over the left parietal lobe; it was firmly attached to the dura mater and measured about 6 by 10 cm. in transverse diameter. Brain-tissue to a depth of about 2 cm. was removed with it. From the description written at the time of the operation, and from subsequent measurements of the trephine opening in the skull, the centre of the portion removed lay over the supramarginal gyrus. He recovered rapidly from the operation, but has since remained under treatment, as he is liable, at rare intervals, to convulsive attacks affecting his right side.

CONDITION IN 1909 TO 1911.

The larger number of our observations have been made between June, 1909, and the present time, and in the following account we will summarize his condition during this period. At present he is unable to read or write, but he can carry out simple orders without mistakes; he occasionally fails, however, to comprehend more complex commands and longer sentences. He talks readily and does not as a rule use wrong words. There is no apraxia.

Special senses.—Smell and taste appear unaffected. There is slight middle-ear deafness on both sides, greater on the right than on the left. Vision is now good in both eyes, but there is right homonymous hemianopsia.

Cranial nerves.—The functions of all the cranial nerves are normal, the pupils are equal and react well, and there is no asymmetry of the face at rest or in movement.

Motor system.—The muscles are well developed in both right and left limbs, and there is no rigidity. The grasps are equal when he can look at his hands, but if his eyes are closed the right hand is clumsy and definitely less powerful. Although a right-handed man, he always uses his left hand to tie a knot or to button his clothes. He walks well, but says the right leg tires easily.

Reflexes.—The tendon-jerks are brisk but equal on the two sides, there is no clonus, and both plantar reflexes give flexor responses.

Spontaneous sensations.—He complains that his right hand seems "dull," as compared with the left, but he cannot explain fully in what this difference

consists. This "dulness" extends over the whole right half of the body, but is less on the foot than elsewhere. He has no pain or tingling.

Tactile sensibility.—He can appreciate cotton-wool contacts over all hair-clad parts of both sides of his body, but he says "the touches are plainer" on the normal than on the affected side. On the right palm he frequently fails to recognize such contacts as evoke constant responses from similar parts of the left hand. To von Frey's hairs the tactile threshold is high even on the normal hand; thus although he responds to 21 grm./mm.² he cannot give a perfect series of answers under 35 grm./mm.² On the affected hand he also responds to 21 grm./mm.², but even with 100 grm./mm.² the series of answers is gravely defective. Moreover, increasing the strength of the stimulus does not produce a corresponding improvement in his answers.

Roughness.—As measured with Graham-Brown's instrument, the threshold is found to be the same on the two halves of the body.

Tickling and scraping.—We can recognize no difference in the effect produced by tickling or scraping on the two sides of the body.

Vibration seems to be equally well appreciated on the two halves of the body, but we found considerable difficulty in determining any finer differences, as the relative length of time during which the fork can be appreciated.

Sensibility to pain.—We can find no difference in the thresholds on the two sides to measured prick or pressure-pain.

Thermal sensibility.—We are unable to find any gross differences between the appreciation of temperature on the two sides of the body, and he seems to be able to recognize correctly the relative hotness or coldness of two temperatures on the same side of the thermal scale. Owing to his speech-defect, finer tests, as the determination of the neutral zone, are difficult and unsatisfactory.

Sense of position.—He is unable to recognize accurately the position in which the affected arm is placed, and by Horsley's method the records obtained, when the normal hand seeks the affected index, are much worse than when he points with the affected hand to the normal forefinger. There is also defective appreciation of the position in space of the right lower limb.

Appreciation of passive movement is gravely affected in the whole of the right upper extremity and to a less degree in the right leg. It is difficult to estimate the amount of this defect, as the patient frequently replies that a movement has occurred when none has been made.

Localization is seriously affected on the right hand; this faculty was tested by various methods, but all yielded the same results. As a rule he attempts to localize the spot stimulated, but often gives up at once, saying, "Yes, I feel it, but I have no idea where it is." He frequently moves the finger that is touched, but even then does not succeed in determining which it is.

Compasses.—The power of discriminating the two points is gravely affected on the right hand and arm. Thus a perfect reading can be obtained on

the back of the normal hand with the points separated to 3 cm., but on the right he is completely unable to distinguish them even when they are 8 cm. apart. Moreover, this loss is equally distinct whether the points are applied simultaneously or successively with an appreciable interval of time between the contacts.

The *power of estimating weight*, either on the supported or the unsupported hand, is completely lost on the right side.

The *appreciation of size, shape, form in three dimensions*, and the nature of common objects placed in his right hand, are completely lost, whereas in the left hand he is remarkably accurate to all these tests.

CASE 18.—*To illustrate the application of our methods in a case of cerebral tumour before and after successful operation.*

William S., aged 51, was admitted to the National Hospital on July 21, 1911, under the care of Dr. Tooth, to whose kindness we are indebted for the opportunity of making the following observations. He had had syphilis ten years previously, and his right eye was destroyed by an accident five years ago. He had been otherwise well till May, 1911, when he began to suffer with attacks of pain of short duration, "like an electric shock," which always began in his left foot, ascended this leg to the hip, then passed up the left side of his body to his shoulder, and into his left arm and this side of his face. At first these attacks consisted in sensory phenomena only, but from June 7 they were followed by clonic spasms of the left limbs, always beginning in the foot, and jerking of his head to the left. His limbs were weak after each of these attacks, and remained permanently so from early in July. When he came under observation hearing and vision were unaffected, but optic neuritis was commencing; the functions of the cranial nerves were undisturbed and the pupils reacted briskly. The right half of the body was normal but the left limbs were weaker, the leg more so than the arm: they were also slightly rigid and all their movements awkward and clumsy. The left deep reflexes were exaggerated, ankle-clonus was easily elicited on the left side, and the plantar reflex was of the extensor type.

CONDITION OF SENSATION BEFORE OPERATION.

The condition of his sensation was carefully investigated at the end of July and in the beginning of August, but as these observations are less valuable for our purposes than those made after the progressive disease was removed, they will be recorded as concisely as possible.

Spontaneous sensation.—He complains only that his left leg occasionally feels numb, and that "I don't seem to have the proper feeling in the left arm or leg."

Tactile sensibility.—He appreciates all contacts of cotton-wool on the hair-clad parts of the affected side, but says they are "less plain" than on the

normal; he misses many contacts on hairless parts, such as the palm. A definite threshold cannot be demonstrated with von Frey's hairs or with the pressure-æsthesiometer, even to a pressure of 35 gm., and fatigue can be induced with unusual ease over the affected parts.

Roughness.—The same thresholds are obtained on both sides with both Graham-Brown's instrument and the sand-paper tests.

Tickling and scraping evoke a "stronger sensation" on the normal than on the affected side.

Vibration.—The tuning-fork can be appreciated everywhere on the affected half of the body, but the sensation is "less plain" than over normal parts. Moreover, when the fork has ceased to produce a sensation on the left half of the body it can be appreciated for at least five seconds longer, if immediately transferred to the corresponding part of the normal side. The fork also seems to beat faster on the normal side.

Sensibility to pain.—Pin-pricks can be appreciated everywhere, but they appear "not quite so sharp" on the affected half of the body. He does not react excessively from either side. The threshold, as measured with the algesimeter, is identical on the two halves of the body, and the readings of the pressure-algometer show no material difference.

Thermal sensibility is not disturbed on either side.

Sense of position is seriously affected in the left arm and leg, and all segments of these limbs must be moved through considerable angles before passive movement can be appreciated.

Localization is also much affected; when tested with tactile stimuli he frequently said, "I can feel it but I can't be sure where it is."

Compasses.—This faculty is very much diminished. A threshold cannot be obtained on the affected hand, even when the points are applied successively, though the normal palm gives a perfect reading with the points 1 cm. apart.

Appreciation of weight.—He cannot recognize the difference between two weights placed on the hands, supported or unsupported, nor the addition or removal of weights on the affected palm.

The *appreciation of size* is disturbed on the affected hand, but not completely lost. He is unable to recognize the test-objects we generally employ to test the *appreciation of shape*. He can, however, recognize the three dimensional objects.

The *appreciation of texture* is also lost in the affected hand.

OPERATION.

On August 30 Mr. Sargent operated, making a large osteoplastic flap in the right side of the skull, which exposed the upper end of the central gyri. Evidence of disease was at once seen in the postcentral gyrus, and a horizontal incision was made into it at about the level of the upper genu of the fissure of Rolando. Through this incision a large circumscribed, partly encapsulated tumour, measuring 5.5 by 4.5 by 2.75 cm., was removed. Microscopical

examination showed that it was a glioma. It lay in the subcortical white matter near the surface, and apparently not far from the mesial surface of the hemisphere. In its removal a considerable portion of the postcentral gyri above the level of the superior genu of Rolando was necessarily destroyed, but as far as could be seen the operative lesion did not affect any part of the brain in front of the central fissure.

He recovered quickly and satisfactorily from the operation, and his condition in October, 1911, was as follows.

CONDITION ONE MONTH AFTER OPERATION.

The functions of the *cranial nerves* and *special senses* are still unaffected.

Motor system.—There is comparatively little loss of power in the left upper limb; the weakness of grasp is due chiefly to the sensory disturbance. The movements of the limb are clumsy, but their range is not restricted. The left leg is relatively weaker, but all its movements can be executed with fair power through a normal range; it is, however, slightly rigid. He can walk without assistance with a slightly hemiplegic gait, the left limb being advanced by circumduction.

Reflexes.—All the deep reflexes are increased on the left side, but ankle-clonus cannot be obtained. When the left knee is extended the plantar reflex is of the extensor type, but when flexed undoubtedly flexor.

Spontaneous sensation.—He complains of no numbness or tingling in the affected side, but when the hand is touched "it does not feel the same" as the normal side. He generally knows where the arm lies, but when the left foot is under his chair he is less certain of its position.

Tactile sensibility.—He can appreciate all contacts of cotton-wool when rubbed across the affected foot, on both hairless and hair-clad parts, but he always says that the sensation is "less plain" than on the normal foot. But if the cotton-wool is simply brought into contact with the skin without movement he fails to appreciate many contacts on the left side, although he misses none on the normal foot. There is no demonstrable disturbance of sensibility to cotton-wool on the hand.

Examination with graduated hairs, or with similar methods, shows all the phenomena we have already described; fatigue is produced with unusual ease, the sensations persist, and hallucinations disturb the examination. A threshold can be, however, obtained on both the hand and the foot, though increasing the strength of the stimulus does not always give a corresponding increase in the proportion of correct answers.

Roughness.—No difference can be discovered between the power of appreciating roughness on the two halves of the body, and an identical threshold can be obtained from the two hands and the two feet.

Tickling and scraping.—When the affected sole is tickled, he says "it is not so plain" as on the normal side, and the reaction evoked is distinctly less.

Vibration of the tuning-fork is appreciated everywhere; but on the affected hand and foot it does not seem so plain as on the normal side. The shortened

power of appreciating the tuning-fork is no longer so definite as before the operation, but he still insists that on the affected foot it seems to be beating slower than on the normal side.

Sensibility to pain.—There is no diminution of sensibility to prick on the affected half of the body, and identical thresholds can be obtained on both sides.

Thermal sensibility.—The thresholds for heat and cold are the same on the two hands; the neutral zone lies between 27° C. and 30° C. But there is a distinct difference between the two feet; thus, though the neutral zone on the right foot lies between 27° C. and 30° C., it extends from 24° C. to 35° C. on the affected sole. He is generally able to recognize correctly the difference between two temperatures on the same side of the scale, provided they differ by 10° C.

Sense of position.—There is considerable loss of the power of recognizing the position of the left lower extremity, and to a less degree in the distal segments of the upper limb.

Appreciation of passive movement is also defective in the left limbs. Movements of the normal knee of from 1° to 2° , for instance, can be constantly appreciated, but on the affected side no movement under 12° was appreciated, and on several occasions a range of 25° was necessary for recognition.

Localization, as tested by the modified Henri method, is perfect on both the foot and the hand; in this respect he has improved greatly since the operation.

Compasses.—On the normal sole a good reading was obtained when the points were 2 cm. apart, but on the affected side a series of correct answers cannot be obtained even at 10 cm. The difference is much less between the two palms; on the normal hand he could discriminate the two points when 1 cm. apart, and he made no mistakes when they were separated to 3 cm. on the affected palm. He is now able, however, to appreciate the two points when they are applied successively.

Appreciation of weight.—The power of discriminating weights placed on the unsupported hand is obviously defective. There seems to be also a slight defect in the recognition of addition to and removal of weights from the palm, but no definite difference can be demonstrated in the power of discriminating two weights placed one after another on the fully supported hand; it must be remembered, however, that the hand is now very little affected, and that it is impossible to test accurately the discrimination of weights on the foot.

The appreciation of size, shape and form.—The appreciation of size alone can be tested on the foot, and he is certainly slower and less certain in his answers from the affected side; further, the difference between the test-objects must be considerably greater than is necessary on the normal sole. On the left hand, where the disturbance of sensibility is much slighter, he can appreciate size, shape, and three-dimensional form as well as on the unaffected side.

The power of recognizing *consistence* and *texture* can be tested on the hands alone, and here no definite difference can be discovered between the two sides.

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A CASE OF LESION OF THE OPTIC THALAMUS WITH AUTOPSY.

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SINCE the publication of Roussy's monograph on the "Syndrome thalamique" in 1907, very few cases with the clinical features and the anatomical lesions which he identified with this syndrome have been recorded. The only ones of which we know are the two further ones described by Roussy himself, two by Long [4], and one by Winkler and van Londen [10]. These, with Roussy's three original observations, and cases recorded by Dide and Durocher [1], Roque, Chaliér and Cordier [7], and Paillard and Lelièvre [6], make a total of eleven cases recorded since attention has been directed by Dejerine to this type of disease of the optic thalamus. A search amongst the earlier literature, however, shows that similar cases, in which the site of the lesion was confirmed by autopsy, had been published by Edinger [2], Greiff [3], and others.

All these cases conform, more or less closely, to the clinical description given by Dejerine and Roussy, and justify its recognition as a clinical type, though even Roussy's own later experiences have shown that in some respects the definition he gave it was too rigid. The absence of a severe hemiplegia with contractures, and of an extensor response, were among the characteristic features he originally described, but they were present in one of his later cases. On the other hand, involuntary choreo-athetoid movements were originally regarded as a typical feature, but they were absent in two of Roussy's own cases.

Despite these discrepancies there can be no doubt that these cases represent a definite clinical group, and, as *post-mortem* examination has shown, their more characteristic symptoms depend on destruction of a special and definite region of the optic thalamus, that is, the posterior part of its external nucleus.

On the other hand, it must be recognized that this syndrome, which Dejerine and Roussy have described most fully, is probably associated with lesions of this portion of the thalamus only, and that disease of other parts of this mass of grey matter may produce essentially different clinical phenomena.

The following case, in which we had the opportunities of full clinical and pathological investigations, evidently belongs to the Dejerine-Roussy group.

W. H., aged 49, was admitted to the National Hospital on August 23, 1909, into one of Dr. Ormerod's beds, but owing to Dr. Ormerod's absence he was, whilst in hospital, under the care of one of us (G. H.). He was a blacksmith, and had until recent years been in good health. He denied alcoholic excess and venereal infection.

The history he gave of his illness was confirmed and amplified by his wife. The first evidence of any cerebral disease was a temporary difficulty in speech, in February, 1906, from which he recovered completely within three days. He had an attack of "influenza" in the autumn of 1908, but was soon able to resume his work, at which he remained till early in 1909, when he had to cease owing to vertigo and a feeling of general weakness. He had complained since then constantly of these symptoms.

In February, 1909, while talking to his wife, he suddenly fell to the ground and lost the power of movement in his right limbs and the right side of his face, but there was no loss of consciousness. He recovered rapidly and was soon again able to use the right limbs quite well. In June, 1909, he had another similar attack, and a third on July 1. The right limbs were weaker after each of these attacks, but he remained able to move them, though he could not employ his right hand in feeding himself, or in other fine actions. Speech was not noticeably affected and the patient's general mental condition did not alter materially. From the date of the first attack, however, he complained much of headache and vertigo.

On the evening of the day on which he was admitted to hospital he became maniacal and violent and had to be removed to the isolation ward. Next day, however, he was quiet, collected and easy to examine. His mental state improved further and for a few days he remained in a condition fairly suitable for our investigations.

He was a sallow, lean man with marked arcus senilis, rigid arteries and a high pulse tension; his heart was hypertrophied, and his urine was of low specific gravity and contained a small amount of albumen. He appeared much older than his age. His memory was poor, and, as he was inclined to become inattentive after a time, it was necessary to interrupt the examination frequently. There was no trace of aphasia or apraxia.

His ocular movements were normal: the pupils were equal but small, and inactive to light. The movements of the jaw were unaffected, and there was no

weakness or asymmetry of the face in either volitional or emotional movements. His palate and tongue moved straight, and there was no alteration of articulation, phonation, or deglutition. Visual acuity was R. $\frac{6}{34}$, L. $\frac{6}{12}$, but there was no hemianopia. Ophthalmoscopic examination, however, revealed severe disease of the retinal arteries, and occlusion of the upper temporal artery of the left eye. Associated with this vascular disease were oedema, hæmorrhages and extensive degeneration of the retina, sufficient to account for the visual deficiency. Hearing, too, was defective, and according to his wife it had been so since the stroke in February, 1909. He was very deaf in his left ear, but on the right side he could hear the tick of a watch by aerial conduction, but not through the bone.

Motor system.—The left limbs were unaffected.

The muscles of the right arm were equal in size to those of the left, but their tone was slightly increased, though the limb could not be described as rigid. Its various movements were unrestricted in range and there was no tendency to contractures. It was difficult to estimate the actual power of the limb as, owing probably to the sensory loss, he seemed unable to exert a constant effort with it; but there was very little, if any, true weakness as compared with the left arm. All its movements were, however, slow, awkward and ataxic, even when controlled by vision, and extremely erratic when his eyes were closed.

There was also slight increase of tone of the muscles of the right leg, but no tendency to contractures or limitation of movement. The same difficulty was met with as in the arm in estimating the strength of the limb, but there seemed to be little or no weakness. Its movements were very awkward and ataxic. He walked with short, uncertain steps, holding the right leg rigidly extended as though it were spastic.

Reflexes.—The deep reflexes were all brisk but equal on the two sides. The abdominal and cremasteric reflexes were also equal, and the plantar reflexes of both sides were characteristically flexor in type.

Spontaneous sensations.—It was difficult to obtain from the patient a full description of his sensations, but he complained constantly of pains and soreness in his right arm, chiefly in the hand and forearm, and in the right foot. These pains were "as if you were bending up the arm and crushing it," or "as if you were breaking it." He also complained of sharp shooting pains in the right side, which usually started in the leg and shot up this side of the trunk into his head; he would frequently grasp his head between his hands and shriek out with pain. He suffered also with "an aching, crampy feeling" in his right limbs and the right side of his body.

Tactile sensibility.—He failed to recognize ordinary cotton-wool touches on the right limbs and on the right side of his trunk, though he responded immediately to even the lightest touches on the left side. Occasionally he appreciated contacts "faintly" on the hair-clad parts of the right side of his face, but not on hairless regions, as on the forehead. On the trunk the anæsthesia to cotton-wool extended almost to the middle line, but by using

slighter stimuli, as a von Frey's hair of 23 grm./mm.², it was found to extend at least 1 cm. beyond it. When a wisp of cotton-wool was rubbed repeatedly and firmly over hair-clad parts of the limbs he could occasionally recognize the stimulus, but vaguely and "faintly." No tactile hairs up to 100 grm./mm.² could be appreciated anywhere on the right arm, the right side of his trunk, or on the right leg, but contacts with a stimulus of this strength could be felt on the right foot, where the sensory loss was certainly less profound than on the rest of this side. Similarly, firm touches with the pulp of a finger or with any blunt object could not be recognized on the right side, except on the foot and the lower part of the leg.

Corneal sensibility.—When tested with von Frey's hairs it was found that, while on the left cornea even 12 grm./mm.² evoked a sensation and a considerable reaction, on the right no hair below 21 grm./mm.² produced a sensation, and even this excited only a slight reflex.

Localization of contact could not be tested owing to the gross defect of tactile sensibility, but in testing painful sensibility it seemed that the patient could localize, at least approximately, pricks that evoked pain.

Compasses.—Records could be obtained from the soles only, as this was the only part of the right side where contacts could be appreciated when the points were applied with reasonable pressure. A perfect series of answers was obtained on the left sole with the points 5 cm. apart, but on the right sole he failed constantly to recognize the double nature of the stimulus even when the points were separated to 10 cm.

Vibration.—He could only appreciate vibration on the right limbs and the right side of the trunk when the fork (C. 128) was vibrating strongly, and when it had apparently ceased to vibrate on this side he could feel the vibrations again for a considerable period if the fork was immediately transferred to the corresponding part of the left side. The diminution of sensibility was less on the leg and foot than elsewhere on the affected side. When asked to compare the sensations evoked on the two sides he said the vibrations "felt louder" on the left than on the right side.

Sensibility to pain.—There was almost complete insensibility to pin-pricks on the right arm and on this half of the trunk; it was impossible to evoke pain even by pricking him repeatedly on the one spot with a sharp pin. On the trunk the analgesia extended to within 1 cm. of the middle line, but apparently pricks did not become naturally sharp until the middle line was crossed. The right side of his glans penis was also insensitive to prick.

On the right leg, especially on its distal segments, pricks could evoke pain, but to do so they had to be stronger than was necessary on the opposite side; the threshold was certainly considerably raised. The pain evoked was generally not so severe as that produced by a similar prick on the left foot, but it was accompanied by a greater reaction.

The greater part of the right side of the head was insensitive to prick, but on the cheeks, lips, and on the forehead just above the eye, even gentle pin-pricks evoked pain.

It is noteworthy that a series of pricks on the one spot of the right arm would occasionally start a movement, though the patient showed no discomfort, and as a rule did not intimate, even when questioned, that he was aware of any stimulus.

Pressure-pain.—It required considerably more pressure with the algometer to elicit pain on the right than on the corresponding parts of the left side, but the discomfort that was then produced, and the reaction it caused, were unquestionably greater on the affected side. A striking feature of these observations was that the pain seemed to appear suddenly or explosively and did not develop gradually as it did on the normal side. The following figures give the approximate pressures that evoked pain on the two sides:—

		R.			L.		
Palm		15	12	11	8	8	8
Temporal fossa	..	5½	4	3½	2	2	2
Sole		9	9	10	5	4	4½

Thermal sensibility.—On the right hand and arm there was complete loss of the appreciation of temperature as such, and the patient reacted only to the disagreeable elements of extreme temperatures. Stimuli between 20° C. and 55° C. evoked absolutely no sensation, but when tubes below 20° C. or above 55° C. were applied to the hand or arm they produced a very intense reaction, the patient withdrawing his hand vigorously, screwing up his face as if in extreme pain, and crying out, "Oh, something has caught me," or "Something is forcing its way into me," or "It's got hold of me; it's pinching me."

The loss of thermal sensibility was very similar on the right side of the face, though he seemed to recognize heat as such, when the temperature was relatively high, in the neighbourhood of the eye. There was also complete loss on the right leg, but on the sole temperatures above 55° C. gave him a sensation of heat; ice, on the contrary, evoked only "a crampy pain," which spread up his leg.

The painful sensations evoked by hot tubes and ice persisted for a considerable time after the stimulus was removed, and according to the patient's description spread widely from the spot stimulated. A tube at 55° C. applied to the sole, for instance, produced a pain that radiated "all over the foot." Equally striking was the fact that the application of high or low temperatures had to be of a considerable duration, occasionally as much as thirty seconds, before the pain developed; then, like the pain produced by pressure, it appeared explosively.

Sense of position of the right limbs was completely abolished; he had no idea how or where they lay when his eyes were closed. This was easily demonstrated by requesting him to place his left (sound) forefinger on his right hand or foot, or to indicate the position of the latter by pointing with the left hand; in seeking his right arm he merely waved the left about until he found his shoulder, and then traced the arm to the hand.

Appreciation of passive movement was also completely lost in the right limbs; he was, in fact, unable to recognize any change of position of these limbs at any of their joints.

Appreciation of weight.—A fairly good threshold could be demonstrated for the left hand, but even the presence of 100 grm. could not be recognized on the right hand, whether it was supported or unsupported.

Other sensory faculties, as the ability to recognize size, shape, and form, could not be tested owing to the serious disturbance of tactile sensibility.

The above notes were completed on September 1. The patient's condition, both mental and physical, then deteriorated so much that no further systematic investigations could be carried out, but we succeeded in confirming many of the facts recorded above.

He died on September 9, and a complete autopsy was performed eleven hours later.

Post-mortem Examination.

The heart was considerably enlarged, owing chiefly to hypertrophy of the left ventricle, but its valves were normal. There was remarkably little disease in the aorta, but many of the smaller vessels were thickened and atheromatous. There was some hypostatic congestion of the bases of the lungs, but they were otherwise normal. The other viscera were free from disease, excepting the kidneys which were small, shrunk and firm; the capsules when stripped off left an extremely granular surface, and on section the cortex appeared very narrow. On microscopical examination the usual features of a small cirrhotic kidney were discovered.

The spinal cord appeared large and well formed. There was no meningitis or other disease visible on the surface, and no degeneration could be detected by the naked eye in its cross-section.

The meninges of the brain were normal except for a slight thickening at the base and on the lips of the Sylvian fissures. The internal carotid and the vertebral arteries were thickened, irregular in lumen and atheromatous, and the larger branches of the circle of Willis, excepting the anterior cerebrals, were similarly diseased. The brain itself was firm, large and well developed. No softening or other disease could be detected on its surface. It was immediately placed uncut into 10 per cent. formalin in normal saline solution for preliminary hardening.

Microscopical Examination.

The spinal cord was examined at various levels by both Marchi's and Weigert's stains, but no systemic degeneration or other disease could be detected in it by either method.

The brain-stem.—When the brain was hardened by formalin the

brain-stem was separated off by a transverse section through the anterior quadrigeminal bodies. One thin slice taken from this region, and another from the middle of the bulb, were treated by Marchi's method; the rest was examined in almost serial sections by Weigert's stain.

In the sections of the mid-brain prepared by Marchi's method there was visible in the middle third of the left pes, in the ordinary position of the pyramidal tracts, a slight amount of degeneration. There was also secondary degeneration of some of the dorsolateral fibres of the left dorsal longitudinal bundle, and a considerable amount of degeneration in the whole cross-section of the mesial fillet. The latter was characterized by a remarkable fineness of the Marchi granules. No degeneration was visible in the other tracts of the mid-brain. In the Marchi sections of the medulla oblongata only a few degenerated fibres were visible in the dorsomedial portion of the left pyramid and some degeneration, represented by very fine granules, in the interolivary layer. On the other hand, no degeneration or disease could be detected in the sections stained by Weigert's method.

There can be no doubt that the slight degeneration of the pyramidal tracts revealed by Marchi's method was due to involvement of certain of its fibres by the lesion that lay on the mesial side of the internal capsule. The degeneration of the mesial fillet contrasted with this by the much finer Marchi granules that represented it, and it is certainly to be regarded as a retrograde or cellulo-petal change, due to the affection of the distal portions of its fibres at or near their termination in the optic thalamus, rather than a true secondary or Wallerian degeneration. This retrograde atrophy or degeneration of the fillet has been repeatedly observed after such lesions. This view is confirmed by the fact that the systematic examination of the rest of the bulb failed to reveal any local lesion that could account for secondary degeneration of the fillet.

The fore-brain.—The fore-brain was cut by sections in the plane of the optic tracts into slices about 1 cm. in thickness. To the naked eye no disease was visible in the right hemisphere, or in the cortex or subcortical white matter of the left, but a focus of softening was at once detected, which appeared in the more posterior sections immediately on the inner side of the external geniculate body and extended from here forwards, through the lateral portion of the optic thalamus, adjacent to the internal capsule.

Those blocks which contained the cerebral end of the mid-brain, the optic thalamus and the corpus striatum, as well as the greater part of

the rest of the left hemisphere, were then mordanted in Müller's fluid, embedded in celloidin, cut in serial sections and stained by Weigert's or by the Weigert-Pal method. The accompanying photographs show the site and extent of the disease that was discovered, and consequently a short description will suffice.

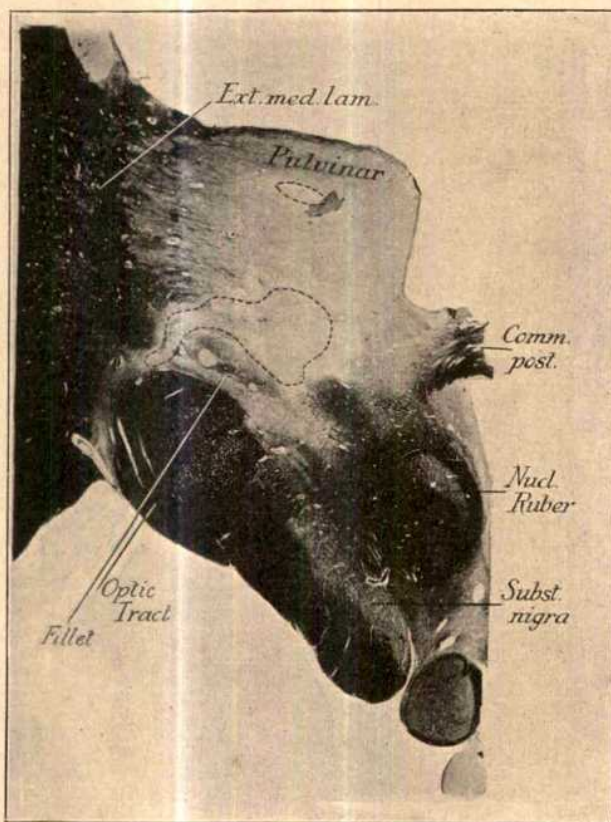


FIG. 1.—Section through the level of the posterior commissure. The softening, as it appeared under the microscope, is outlined by a broken line. Another small focus of softening lies in the dorsal part of the pulvinar.

The caudal extremity of the lesion, which extended just below the section shown in fig. 1, lay immediately mesial to the external geniculate body and to the dorsolateral angle of the pes, but neither of these structures was definitely affected by it. It spreads mesialwards into the inferior portion of the pulvinar, but not further ventralwards than the level of the posterior commissure. A little higher, at the upper

end of the external geniculate body (fig. 1) it lies chiefly in the ventral portion of the pulvinar, but its lateral angle projects into the lamina medullaris externa immediately dorsal to the crus. At this level the mesial fillet, as it bends dorsolateralwards into the thalamus, lies immediately ventral to the lesion, but is not here directly involved by it. It appears, however, poorly stained and atrophied. There is also slight rarefaction in the outer third of the pes, but this is otherwise normal.



FIG. 2.

The lesion occupies the same relative position in the succeeding sections but becomes larger. In a section through the ganglion habenulæ and the corpora mammalaria (figs. 2 and 3), its main portion lies ventral to the anterior end of the pulvinar and extends mesialwards to about the plane of the lamina medullaris interna, and ventralwards into the ventral nucleus. Its lateral portion at first projects almost

horizontally outwards, breaks through the lamina medullaris externa into the reticular zone of the thalamus, and there spreads in the plane of the section along the inner margin of the internal capsule. The latter, however, is not directly invaded by the softening, and no degeneration can be detected in it by Weigert's method.

At this level, and slightly above it, that portion of the ventral nucleus of the thalamus in which the fillet terminates is invaded by

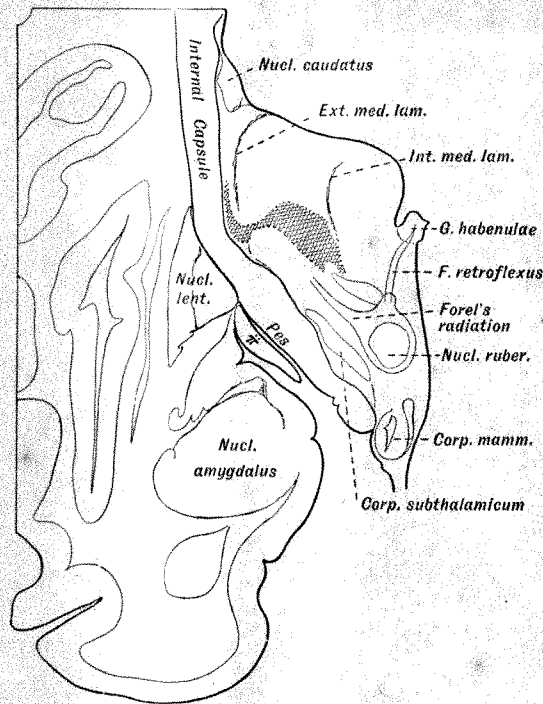


FIG. 3.—A drawing of the section shown in fig. 2, under a lower magnification. The lesion, as seen under the microscope, is cross-hatched.

the lesion. To this, and more especially to involvement of some of its fibres, the retrograde atrophy of the fillet must be attributed.

As the lesion is traced upwards its ventromesial portion becomes smaller, while the lateral part is larger (fig. 4), and extends vertically through the lateral zone of the thalamus. The mesial part extends inwards to the lamina medullaris interna, but leaves the mesial nucleus almost intact; while its lateral portion forms a narrow strip in the reticular zone, extending dorsolateralwards almost to the caudate

nucleus, and ventromesialwards to the lateral angle of the corpus subthalamicum. At this level in fact it runs more or less parallel with the internal capsule, and separates the thalamus from it. It maintains this form and position almost to the dorsal surface of the thalamus, but in the highest sections of this (fig. 5) it is not quite continuous, but is represented by two distinct foci in the reticular zone and the lamina medullaris externa.

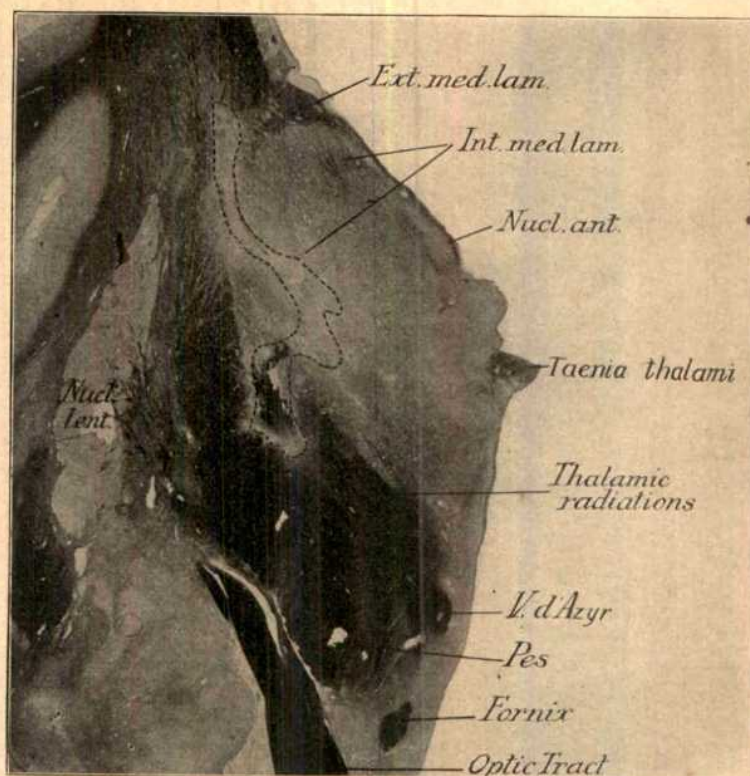


FIG. 4.—The lesion is outlined. It contained at this level in its ventral part a relatively recent hæmorrhage.

The internal capsule was not actually involved by the lesion at any level, though here and there its fibres appeared rarefied where the lesion impinged upon it.

The lesion consisted of a softening with complete destruction of the cells and fibres within it, and their replacement by loosely proliferated neuroglia. Its limits were easily definable, but in places it appeared as

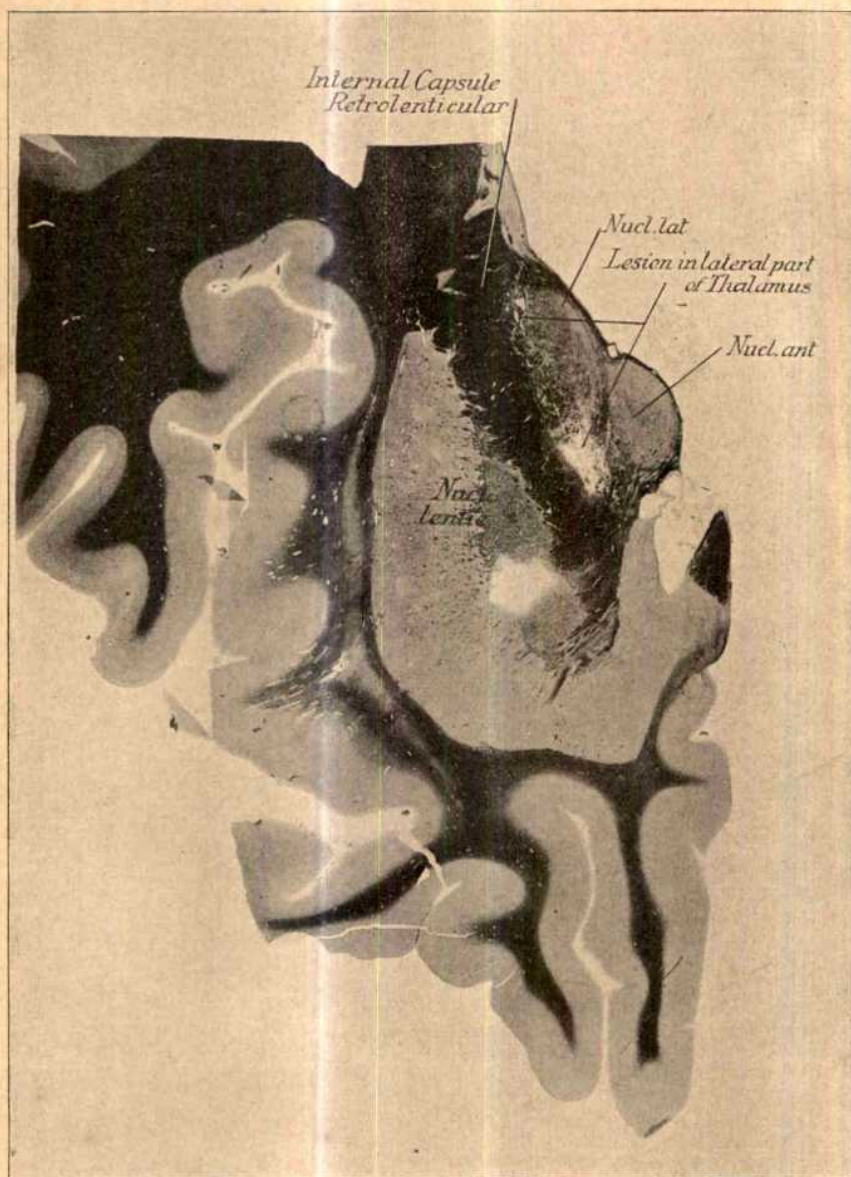


FIG. 5.—The softening in the lateral nucleus is here represented by two foci. A small patch of softening also lies in the nucleus lenticularis.

if the vascular occlusion that produced it had caused a necrosis of tissue more extensive than the actual softening. It was consequently necessary to outline its actual extent in the photographs that serve as illustrations. In one place (fig. 4) the softening contained traces of a relatively recent hæmorrhage.

The only other focus of disease, excepting a minute softening in the dorsal part of the pulvinar (fig. 1), was a small patch of softening, shown in fig. 5, in the lenticular nucleus on the outer side of the genu of the internal capsule.

The cortex of the central convolutions was examined by Nissl's method, but no definite pathological changes were discovered.

We can *summarize* this case as follows: A man, aged 49, with chronic Bright's disease and hypertrophy of the heart, suffered from three strokes at short intervals, without loss of consciousness, the last more than two months before his death. There was little or no paralysis, and the reflexes remained normal, but he suffered with severe pains throughout the whole of his right side, associated with almost complete loss of tactile and postural sensibility on this side. The threshold for painful stimuli was much raised, though certain forms of discomfort, when evoked, were more severe, less bearable, and produced a greater reaction. The appreciation of temperature was abolished, but thermal stimuli below 20° C. and above 55° C. produced more discomfort than on the normal side, and an excessive reaction. There was also loss of the ability to appreciate weight, size, shape and form. He had bilateral deafness, greater on the side opposite to the lesion, as a result of the strokes.

On *post-mortem* examination an extensive softening was found in the ventral and lateral regions of the left optic thalamus, which invaded that portion of the ventral nucleus of the thalamus in which the fillet terminates. The greater portion of the softening, however, formed a narrow cleft in the lateral zone of the thalamus separating it from the internal capsule. The internal nucleus of the thalamus was very little affected.

It is evident that both the clinical symptoms and the anatomical lesion in this case conform closely to those of the type described by Dejerine and Roussy. It will be therefore interesting to collate the symptoms we observed in this patient with those of similar cases, in which the site and extent of the disease was determined by autopsy. For this purpose we may refer particularly to those recorded by Edinger,

Greiff, Roussy (five cases), Long (two cases), and Winkler and van Londen. The cases published by Roque, Chaliér and Cordier [7], and by Paillard and Lelièvre [6], ended in death so early after the onset of the lesions, that the effect of shock on their symptomatology cannot be excluded. In that recorded by Dide and Durocher [1] the exact extent of the lesion was not determined by microscopical examination.

Roussy defined the "syndrome thalamique" by the following symptoms and signs: hemianæsthesia, involving deep sensibility more than the superficial forms, with persistent, paroxysmal, spontaneous pains on the affected side; little or no hemiplegia; hemiataxia, and frequently irregular involuntary movements of the athetoid or choreic type, in the affected limbs.

Our case presented all these symptoms except involuntary movements, but on analysing the ten cases referred to we find that this symptom was present in four only of them (Roussy [8], obs. 1, and [9], obs. 1; Edinger and Greiff). Consequently, it cannot be regarded as an essential clinical feature of this group, though it is undoubtedly highly characteristic when it occurs. Hemiataxia, which was pronounced in our case, is apparently a more frequent symptom; it was definitely recorded in seven of the ten cases.

The sensory loss in our case was greater than in most of those we refer to, but in this respect it closely resembles one of Roussy's ([9] obs. 1). The sensory disturbance, however, speaking merely of these ten cases, is very variable in its intensity and, as Roussy has shown, affects chiefly what he calls "deep sensibility," that is, the postural elements. In another of his cases, for example ([8] obs. 3), the appreciation of touch, pain and temperature was unaffected, and the sense of position and the recognition of form alone were lost. In Edinger's case, on the other hand, the sense of position was undisturbed, and there was only an over-reaction to certain stimuli.

Spontaneous pains and paræsthesiæ, which were a prominent feature in our case, are more constant and characteristic, and were, in fact, absent in two only of the ten cases (Roussy [8] obs. 2, and Winkler and van Londen).

But there is another clinical feature of these cases which has not hitherto attracted special attention, though its occurrence has been frequently mentioned in the clinical descriptions; this is a tendency for certain stimuli, generally of the unpleasant order, to produce more pain and discomfort on the affected than on the normal side

of the body, despite the diminution of sensibility. In our own case almost all stimuli that could evoke a sensation had this effect; pricks when they affected consciousness, it is true, produced only a greater reaction, but sensibility to this form of stimulation was very low. With painful pressure, however, the excessive discomfort and reaction were very pronounced; while high and low temperatures, which were recognized only as painful or unpleasant stimuli, had the same effect. Roussy refers to this phenomenon as "dysesthésie." In his first case ([8] obs. 1) prick evoked numbness and disagreeable sensations: there was "hyperæsthesia" to cold, and even the tuning-fork produced a sensation of "intense burning." In a second case ([8] obs. 2) prick produced a painful numbness that was badly localized, and heat above 50° C. evoked pain. In another case ([9] obs. 1), he observed that tickling was extremely unpleasant to the patient, and in his last recorded case ([9] obs. 2) even stroking the skin or hairs was painful, and thermal stimuli evoked tingling. In Edinger's case even touch was painful and cold was unbearable, and in Greiff's hyperæsthesia was observed. Winkler and van Londen found that pinching or squeezing evoked "a much sharper perception of pain" on the affected than on the normal side, and this was associated with "vehement repelling movements." In fact, in two only of these ten cases, in those recorded by Long, was there no mention made of this tendency for affective stimuli to evoke pain and discomfort.

We have discussed elsewhere the significance of this phenomenon, which we regard as the most constant and characteristic feature of lesions of the lateral zone of the optic thalamus, and need not enter on it here again. We may only mention that we discovered it in some form or other in all the twenty-four cases of thalamic lesions that we have studied clinically.

Another symptom in our case, unhappily one that was not carefully investigated, was a partial deafness which, according to the history, supervened on the attacks that produced his other symptoms. It was bilateral, but greater on the side of the lesion. Owing to the incomplete examination of the ears we cannot exclude local or other causes of this deafness, but as it has been observed in other cases it deserves a short reference. In two of his cases ([8] obs. 1, and [9] obs. 2), Roussy merely records slight diminution of hearing on the same side as that affected by the other symptoms, and no further analysis of the nature of the defect was made. In Winkler and van Londen's case almost complete deafness followed on the lesion, but hearing

returned partially; and in Greiff's case hearing was diminished on both sides. We also found defective hearing in several of the clinical cases we have investigated; in some its occurrence was definitely associated with the stroke that produced the other symptoms, and its nature suggested that it was of central origin. The most interesting communication on this point is that published by Merle [5]; for in his case partial bilateral deafness, greater on the side of the sensory symptoms, followed immediately on the stroke, and as in a case that we have observed, was associated with extreme susceptibility to loud sounds and noises, which became actually painful to the patient. This phenomenon, as Merle points out, is analogous to the over-response to certain sensory stimuli that also occurs in these cases.

The affection of hearing has been generally bilateral, though usually greater on the side opposite to the lesion. Its occurrence is easily explicable by the site of the lesion, for when situated in the posterior and lateral part of the optic thalamus it may involve the internal geniculate body itself; or, as in Winkler and van Londen's case, it may interrupt the cortico-petal fibres from the internal geniculate body as they pass through Wernicke's zone.

Finally, we may point out that the disease in our case occupied approximately the same site as the lesions in other cases with similar symptoms. According to Roussy, the characteristic lesion destroys the posterior third of the lateral nucleus, and parts of the internal nucleus, of the centre median and of the pulvinar; and these were the portions of the thalamus that were actually affected in our case. But perhaps its most striking feature was that the internal capsule and the crus escaped almost entirely despite the size of the lesion; in this respect it resembles most closely the cases of Edinger, and of Winkler and van Londen. The thalamic lesion in our case, too, was probably larger and more extensive than in any instance yet recorded, as it reached from the lateral geniculate body to the nucleus anterior thalami; and yet it left the internal division of the thalamus almost entirely intact.

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THE RESPONSE OF NORMAL AND ABNORMAL MUSCLE TO LEDUC'S INTERRUPTED CURRENT.

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AT the Congress of the French Association for the Advancement of Science, held at Angers in 1903, Professor S. Leduc, of Nantes, described a form of electrical current, the aim of which was to produce a given excitation with a minimum expenditure of energy. It consists of a galvanic current, rapidly interrupted, and with the "make" forming a definite known proportion of each period. For its production he devised a special interrupter (driven by an electric motor), which is fully described and figured in the *Archives d'Electricité Médicale* (Bordeaux), November 25, 1908. It enables the current to be interrupted at rates of 20 to 200 per second, the frequency being recorded by a special counter attached. Further, in each resulting period the time of "make" can be varied from $\frac{1}{100}$ to $\frac{70}{100}$ of the total period. The current thus obtained may be represented graphically by the annexed diagram (fig. 1).

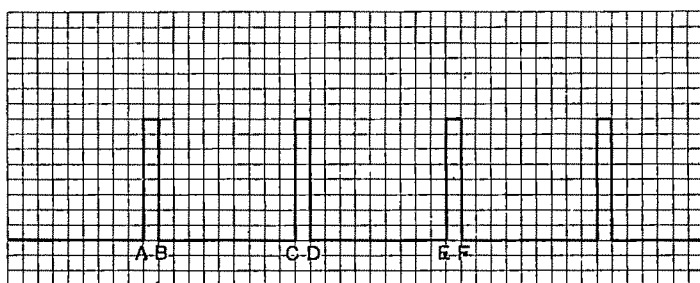


FIG. 1.—Scheme of current obtained with Leduc's Interrupter. In this figure, each period of "make," AB, CD, EF, is $\frac{1}{10}$ of the total period, AC, CE, &c.

The duration of each complete period (make and break), AC, CE, &c., varies from $\frac{1}{20}$ (.05) second to $\frac{70}{200}$ (.005) second. In each such

period, the ratio AB/AC , CD/CE , &c., can be regulated between the limits $\frac{1}{100}$ and $\frac{70}{100}$. It follows, therefore, that the actual duration of each contact can be varied from $\frac{1}{100}$ of $\cdot 005 = \cdot 00005$ second to $\frac{70}{100}$ of $\cdot 05 = \cdot 035$ second.

By the use of this current, the phenomena usually associated with the faradization of muscle can be reproduced, with this added advantage, that all the factors of the stimulating current are susceptible of direct measurement and delicate gradation. Thus the strength, duration and frequency of the stimulus are all under control, and can be varied independently of one another. As suggested by Leduc (*op. cit.*), this type of current should be eminently serviceable for the clinical examination of human muscle. It was for the purpose of obtaining the requisite data for such clinical employment that the experiments described below were performed.

I.—THE RESPONSE OF NORMAL MUSCLE.

As these experiments were made with a view to applying the results to man, it was, of course, essential to use mammalian muscle for the purpose. In every case cats were employed, and were kept fully anæsthetized throughout the experiment. Two sets of muscles were investigated: (a) a flexor group—the soleus-gastrocnemius; (b) an extensor group—the quadriceps of the thigh. The results were practically identical in the two cases; the former was, however, a more convenient preparation to work with, so most of the experiments were done with it. Except where otherwise stated, the results here detailed were obtained from the gastrocnemius.

The preparation was made as follows: The skin of the calf was reflected, care being taken to avoid hæmorrhage from the large superficial veins. The calf-muscles were then freed from the musculo-tendinous expansions of the hamstrings which run down on either side towards the tendo Achillis. The latter was then separated from its bony attachment, and the superficial muscles (soleus and gastrocnemius) carefully dissected from the deep flexors, nearly up to their origin. The tendo Achillis was then connected by a suitable thread to a "Keith Lucas Rectilinear Myograph" (weighted with 50 to 120 grm.), arranged to write on the smoked paper of a kymograph. Two platinum-iridium wire electrodes were then passed through the upper and lower parts of the muscle, and connected to the kathode and anode of the stimulating circuit. During the whole experiment the muscle

preparation was kept warm and moist by irrigation with "normal saline" at body temperature.

The source of the current was the main supply (220 volts continuous, passed through a lamp resistance, and a suitable rheostat for grading the voltage). This was in series with a milliamperemeter and a Leduc Interrupter (made by Gaiffe, of Paris), with special counter attached. The circuit, which also contained a "Post-Office" make-and-break key, was completed by the wire electrodes.

As regards the measurement of the current, the amperemeter gave a steady reading with all rates of interruption from twenty per second upwards. If each "make" was $\frac{x}{100}$ of the total period, then the reading would be $\frac{x}{100}$ of the actual current. Thus, with the scale at 10 ("make" = $\frac{10}{100}$ of each period), a reading of .2 milliampere corresponds to an actual current of 2 milliamperes (uninterrupted).

The tracings were taken on a stationary drum which was moved by hand between each observation. The contractions were obtained by momentarily pressing the make-and-break key. In addition, a series of contractions were recorded on a moving drum, with the usual signal to register the period of stimulation.

Results.

(In all the succeeding matter, the fractions $\frac{1}{100}$, $\frac{2}{100}$, $\frac{x}{100}$ may be taken as referring to the ratio make: total period, as previously indicated.)

Fig. 2 represents the typical response of normal muscle to the Leduc current, with constant ratio of make: total period (in this case $\frac{10}{100}$), but with varying frequency of interruption. It will be seen that, as the frequency of interruption is increased from 20 to 120 per second, the heights of contraction increase; from 120 to 200, the heights are approximately equal, though there is a slight tendency to diminution. A large number of experiments of this type was made; in every case the increase with increasing speed was obtained, though the *optimum frequency* was not quite constant. It varied between the limits of 90 and 120. Thus in fig. 3 the maximum contraction is obtained at 100. This tracing shows another point of interest, namely, the more marked decrease obtained as the frequency was increased from 100 to 200. This was noted in several cases, though the majority of tracings obtained were of the type shown in fig. 2. It may be noted then, that all agree in the initial rise to a maximum between the limits 90 and

120, but that there is a divergence as regards the shape of the remainder of the tracing. In some, the gradient of decline is considerably more marked than in others. The significance of this difference will be discussed later.

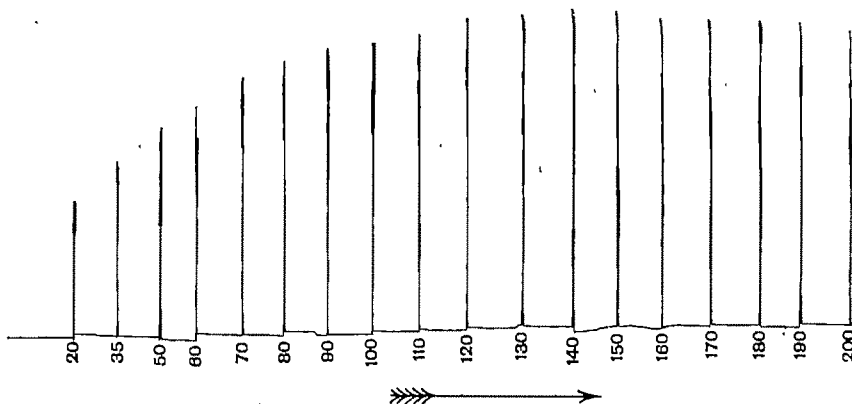


FIG. 2.—Normal gastrocnemius; tracing of contraction, with constant ratio $\frac{18}{100}$, and gradually increasing frequency of interruption (figures below curves of contraction represent the number of interruptions per second). From L. to R.

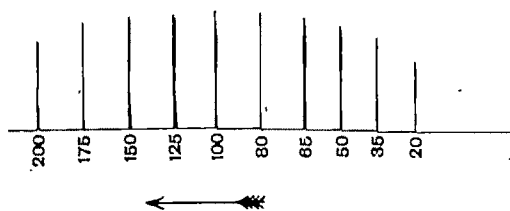


FIG. 3.—Normal gastrocnemius (cf. fig. 2). This tracing shows the tendency seen in some cases for the contractions to diminish with increasing frequency. From R. to L. (See text.)

If the frequency, instead of being increased from 20 to 200, is diminished, step by step, from 200 to 20, the tracing obtained is the negative image of those just described—i.e., the relation of height to frequency is the same. Further, it is independent of the ratio make : total period, as long as this does not fall below $\frac{1}{100}$ (v.i.). Nor is it affected by changes in the strength of the current; provided this is submaximal, the curve shows the same features with varying strength of current.

Fig. 4 shows the result of stimulation of the trunk of the sciatic nerve with a very weak current, $\frac{5}{100}$, at varying frequency. In this, the relation of height of contraction to frequency of interruption is not unlike fig. 2; it differs, however, in having its optimum frequency at about 170, instead of 120.

In a current employed in the manner indicated, in which the ratio $\frac{x}{100}$ remains constant, while the frequency of the interruption varies, there are really two variable factors to consider: (a) the absolute duration of each "make" period; (b) the frequency of interruption.

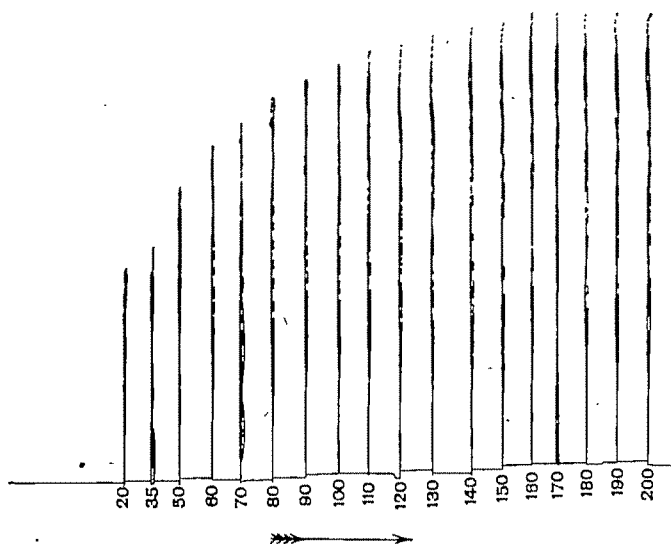


FIG. 4.—Normal gastrocnemius: contractions obtained by stimulating the sciatic nerve with very weak current; contact ratio $\frac{5}{100}$; gradually increasing frequency.

Thus, when the make is $\frac{10}{100}$ of each period, its actual duration at a frequency of 20 per second is $\frac{1}{2000} = .005$ second, while, with a frequency of 100 per second, this is reduced to $\frac{1}{10000} = .001$ second. Hence it follows that, in the experiments just described, the duration of each "make" diminishes proportionately with the increase of frequency. Consequently a series of observations was made with a view to estimating separately the influence of these two variables.

(a) *Keeping the Frequency constant, but varying the actual duration of "Make."*

If the interruptions are kept constant, say at 100 per second, and the ratio $\frac{x}{100}$ is gradually increased from $\frac{1}{100}$ to $\frac{80}{100}$, it is found that

the height of the contractions increases till x reaches 5—i.e., until the duration of each "make" is $\frac{5}{100}$ of $\frac{1}{100} = .0005$ second—thence onwards the contractions remain approximately equal. The same result is obtained if the value of x is gradually diminished from 20 to 1 (fig. 5). The corresponding values of x at other rates of interruption are given approximately in the following table:—

Rate of interruption per second		Minimum value of " x " for optimum contraction (mean of several observations)			Actual period of "make"
50	..	3	..	..	.0006 sec.
75	..	4.5	..	..	.0006 "
100	..	5	..	..	.0005 "
125	..	6	..	..	.00048 "
150	..	7	..	..	.00046 "

It seems, therefore, that for each rate of interruption there is a *limiting value* of "make" period beyond which the efficiency of the current is not increased by increase of its duration.

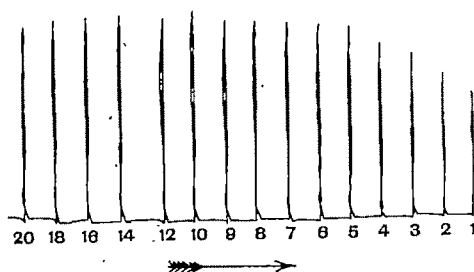


FIG. 5.—Normal gastrocnemius; tracings obtained with constant frequency of 100; ratio $\frac{x}{100}$ gradually diminished from $\frac{20}{100}$ to $\frac{1}{100}$. L. to R.

It is a matter of interest to consider this result from the point of view of Nernst's theories of the stimulating effect of the constant current. He assumes that the exciting effect of such a current can be due to ionic displacement only, and suggests that it is proportional to the changes in concentration of ions at the surface of semi-permeable membranes [6]. He has calculated that the change (c) produced by a constant current (i) of short duration (t) is proportional to $i\sqrt{t}$. In other words, the concentration changes, and therefore the stimulation efficiency, varies as the product of the strength of the current and the square root of the time (see also Keith Lucas [3] and Hill [1]). This formula holds only for very small values of " t "; a limit is soon reached at which "accommodation" occurs, due to a reverse passage of ions

which tends completely to neutralize that due to the current.¹ The upper limit of time for which this formula holds good in the case of the frog's sartorius was found to be '01 second (Keith Lucas) [4].

Now in fig. 5 it is seen that the height of contraction from $\frac{20}{100}$ to $\frac{50}{100}$ are equal. The frequency of interruption was constant (100); hence it is justifiable to assume that the exciting value of each "make" was equal, though their periods varied. In other words, for normal cat's gastrocnemius, with complete innervation, the *limiting time*, above which "accommodation" (in Nernst's sense) comes into full play, is of the order of '0005 second, and therefore very much below the figure obtained by Lucas for the frog's sartorius (see further, below).

It will be noticed that the figures given in the above table show a slight diminution as the frequency increases, being '0006 second for 50, and '00046 for 150. I can give no explanation of this discrepancy, but the figures are sufficiently concordant to serve the purpose for which they are intended to be used (see p. 288).

(b) *Keeping the Period of "Make" constant, but varying the Frequency of Interruption.*

A series of observations was made in which the value of "x" was made to vary directly as the frequency of interruption, as follows:—

Frequency	Value of "x"	Actual period of "make"
20	1	'0005 sec.
40	2	"
60	3	"
80	4	"
100	5	"
120	6	"
140	7	"
160	8	"
180	9	"
200	10	"

Similar observations were made in which the "make" period was kept constant at '001 and '002 second respectively. The results obtained were practically identical in the three cases. Fig. 6 shows the record of such an experiment. It will be seen that the result is very similar to fig. 2—i.e., the size of the contractions increases with increasing frequency up to 120, and then remains approximately constant. This is what one would expect, bearing in mind the results obtained with constant frequency (*v.s.*). For, with a value of $\frac{x}{100} = \frac{10}{100}$, the actual period of each "make" never falls below

¹ This "accommodation" may be compared to that postulated by Hering in his theory of metabolism, in which dissimilation leads automatically to assimilation, and *vice versa*.

the value '0005 second, determined as the "accommodation" limit for this muscle. This factor, the period of each make, does not therefore play any part in determining the size of the contractions; the only other variable is the frequency of interruption, and, as we see, this is in itself sufficient to produce the result shown in fig. 2.

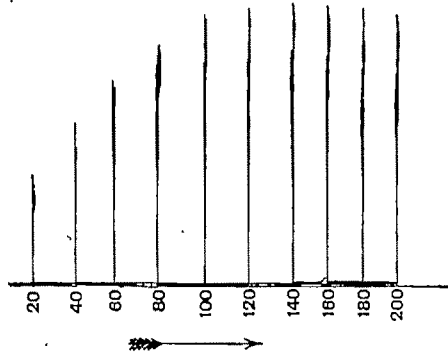


FIG. 6.—Normal gastrocnemius; tracings obtained with constant period of make ('005 sec.), but with varying frequency of interruption (20 to 200).

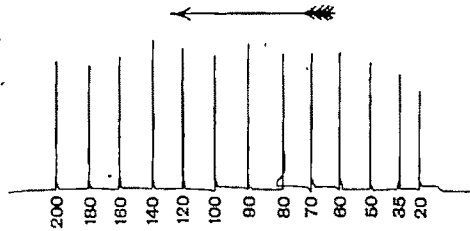


FIG. 7.—Normal gastrocnemius; constant ratio $\frac{1}{100}$; varying frequency from 20 to 200 interruptions per second. R. to L. (See text.)

The conditions are, however, different if, instead of $\frac{1}{100}$, we employ a smaller value—e.g., $\frac{1}{150}$ —and vary the frequency. In this case, as soon as the frequency is increased beyond 20 per second, the actual period of make falls below the limiting value, and becomes progressively more so as the speed is increased. In this case, therefore, there are two variable factors at work, of opposite sign—(a) the increasing frequency, tending to increase the size of the contractions, and (b) the diminishing periods of make, tending to diminish the contractions. Fig. 7 shows the tracing from such an experiment. It will be seen

to differ from fig. 2, in that it fails to show the regular increase to a maximum of 100 to 120, but has an irregularity dependent on the conflicting gradients of these two opposing factors.

II.—THE RESPONSE OF CURARIZED MUSCLE.

To investigate the response of muscle in which the motor end-plates had been paralyzed by curare, a series of observations was made on cats after intravenous injection of a 2 per cent. solution of curare, artificial respiration being maintained by a Brodie's pump (with chloroform in the air-chamber). The efficiency of the injection was always tested by stimulation of the nerve-trunk.

The strength of current necessary to produce a fair-sized contraction was much greater than for normal muscle; the weaker currents produced only a local contraction in the neighbourhood of the electrodes. Further, the shape of curve obtained with constant ratio—e.g., $\frac{10}{100}$ —and gradually increasing frequencies showed a considerable difference from those above considered. Instead of a maximum at 90 to 120, the curarized muscle showed one at 50 to 70, followed by a sharp decline, so that with a ratio $\frac{10}{100}$, and current-strength .6 ma. (*v.s.*), no contraction at all was obtained with a frequency of 200¹ (cf. fig. 8).

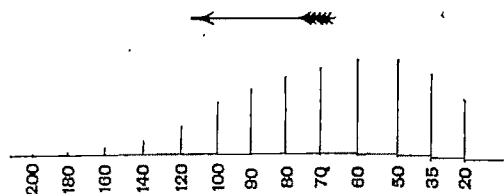


FIG. 8.—Curarized gastrocnemius; tracing of effect of strong current. Ratio $\frac{10}{100}$; varying frequency of interruption 20 to 200 per second. R. to L.

Comparing the curves for curarized muscle, normal muscle, and nerve-trunk, it will be seen that the response of normal muscle is, in a sense, intermediate between the other two—nerve-trunk and curarized muscle. Thus, the optimum frequency for nerve is 170 and onwards (cf. fig. 4), for curarized muscle 50 to 70, and for normal muscle 100 to 120. This suggests that when a muscle is subjected to direct

¹ If, however, the strength of current is sufficiently increased, curarized, like normal muscle, will show definite contraction even with ratio $\frac{10}{100}$, and speed of 200—i.e., with stimuli of only .00005 second duration.

stimulation in the manner described, the contraction is a composite one, resulting partly from stimulation of the intramuscular nerve-trunks, and partly from direct stimulation of the muscle-fibres themselves.

We are now in a position to discuss the significance of the variation noted on p. 274, as regards the optimum frequency of interruption and the gradient of decline (if any) in normal muscle. At first I was inclined to regard the curves of the type shown in fig. 3 as due to damage to the muscle from hæmorrhage, excessive exposure, &c. But the observations detailed in the following section make it improbable that these factors play any great rôle in the genesis of these variations. A more likely explanation is the relative predominance in any particular case of the two factors—nervous and muscular. If a relatively large intramuscular nerve-trunk happens to be near the electrode, then the response approximates more to the “nervous” type, while, if fewer nerve-fibres are stimulated, the response will show an optimum at a rather lower frequency, and a more marked gradient of fall as the frequency approaches the 200 limit.

Curarized muscle shows another difference from normal muscle, of particular interest in view of the results obtained after nerve-section (*v.* Section IV). The “limiting period,” instead of being about .0005 second, has a value about six times as great, about .0033 second. This is shown by the following figures (*cf.* p. 277):—

Rate of interruption per second	Minimum value of “x” for optimum contraction	Actual period of “make.”
50	.. 18	.. .0086 sec.
100	.. 80	.. .0090 „
150	.. 50	.. .0088 „

It cannot, of course, be assumed that these results represent those would be obtained from perfectly normal muscle deprived of its nerve, as one must bear in mind the possibility of a toxic effect of curare on the muscle-tissue itself. Such an effect does not, however, seem to be at all prominent, as was shown by the following experiment: 1.5 c.c. of the curare solution was injected intravenously, and produced complete paralysis of the motor nerve-endings. The response to direct stimulation was as above indicated; 3 c.c. more curare was then injected gradually, and more applied directly to the muscle, but the response was not further affected; it still gave an optimum at a frequency of 60, with about the same gradient of decline with in-

III.—RESPONSE OF EXHAUSTED AND DYING MUSCLE.

After a muscle has been stimulated with strong tetanizing currents for long periods (five to fifteen minutes) the response obtained is somewhat similar to that just described for curarized muscle—i.e., an optimum at a frequency of 60 to 80, and a steeper gradient of decline from this point with increasing frequency. It seems, indeed, that the prolonged stimulation actually causes temporary paralysis of the motor end-plates, as is shown by the fact that if the stimulus is applied to the nerve-trunk the response gradually disappears, to return if the stimulus is then thrown direct into the muscle (by a Pohl's commutator without cross-wires). As a rule, however, the effect produced by this method is not quite so marked as with curare; the optimum never fell to 50, as it did in the case of the latter drug.

This modified response of exhausted muscle is of comparatively brief duration; after two to three minutes the normal response reappears—i.e., the motor end-plates recover their conductivity in this time.

The gradual alterations of excitability in the muscle following the death of the animal were examined in several cases. Immediately after death (by bleeding or pithing), the response shows no deviation from the normal; five minutes later the optimum was still 100, and the gradient of decline with increasing frequency very gradual. The following table shows the approximate findings at varying periods after death:—

$\frac{x}{100} = \frac{10}{100}$		Optimum		Gradient of decline
Minutes after death				
5	..	100	..	Slight
15	..	80—90	..	Slight
20	..	60—70	..	Rather steeper
25	..	50—60	..	" "
45	..	50	..	Steeper
60	..	20—25	..	Steep
90	..	20	..	Very steep (no contraction at frequency than 100 with strong currents)

In other words, after about an hour the muscle of a dead cat behaves in a manner very similar to the "degenerated" muscle resulting from nerve-section.

IV.—THE RESPONSE OF DEGENERATED MUSCLE.

To examine the response of muscle at varying periods after nerve-section, the left sciatic was resected in the middle of the thigh in a

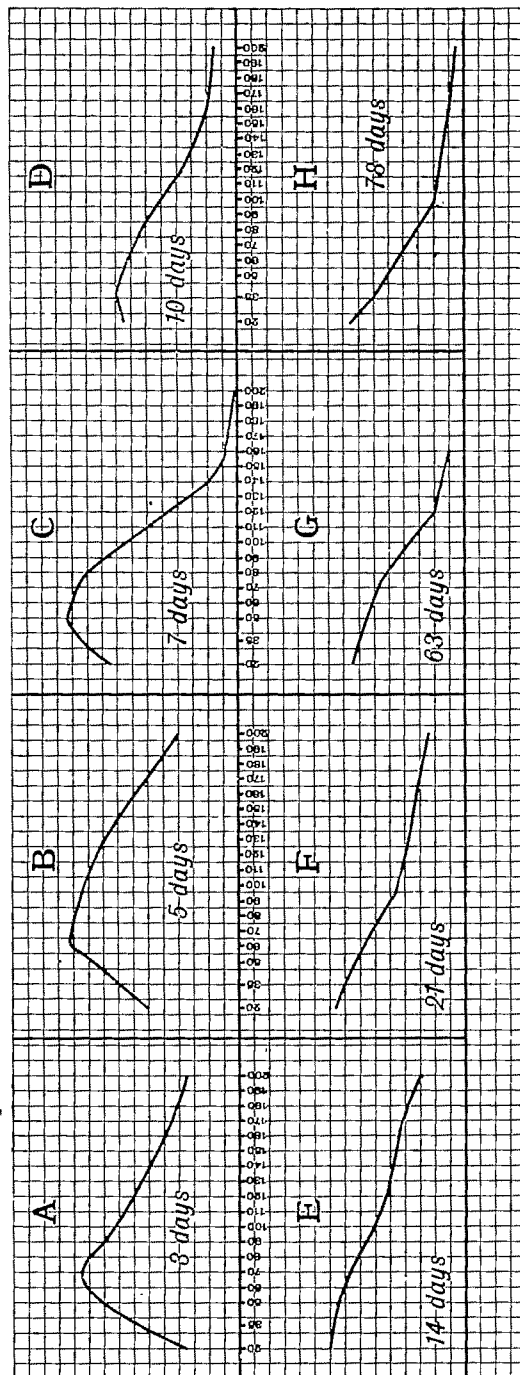


FIG. 9.—Diagram of curves plotted to show relation of height of contraction to frequency of interruption in a series of gastrocnemii at various intervals after sciatic nerve-section. In all, constant ratio $\frac{y}{x}$; frequency of interruption varied from 20 to 200 per second.

series of cats, with strict antiseptic precautions. At a suitable period after operation the gastrocnemius was tested in the usual way.

The results are exhibited graphically in fig. 9, which shows the response to gradually increasing frequencies of interruption, at periods varying from three to seventy-eight days. From this it will be seen that, as the time after nerve section increases, the *optimum frequency* diminishes, until, from fourteen days onwards, the curve falls gradually from the beginning. In other words, when a certain stage of "degeneration" is reached, the best contraction for any given value of $\frac{x}{100}$ —e.g., $\frac{10}{100}$ —is with a frequency of 20; as this is increased, the contractions become steadily less. The following table gives the optimum for various times:—

Days		Optimum frequency
3	..	70
5	..	60
7	..	50
10	..	35—50
14	..	20—35
21	..	20
63	..	20
78	..	20

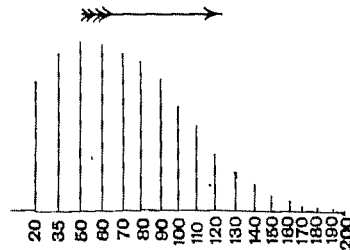


FIG. 10.—Gastrocnemius seven days after sciatic section; tracing of contractions; constant ratio $\frac{x}{100}$; varying frequency of interruption 20 to 200 per second. L. to R.

Fig. 10 is the actual tracing from a gastrocnemius seven days after section of its nerve. A comparison with fig. 2, from a normal cat, shows a striking difference, not only as regards the shifting backwards of the optimum, but still more in the gradient of descent from this point onwards.

The functional change in denervated muscle is brought out equally well by an examination of the results of varying the ratio $\frac{x}{100}$, with constant speed of interruption. Unfortunately this was not completely investigated in all the cases, but the following figures suffice to

show how the "*limiting time*" (in the sense explained on p. 278) is increased in these conditions. In the following table, the frequency of interruptions is 100 in each case.

Days after nerve-section		Minimum optimum value of $\frac{t}{T_{100}}$		"Limiting time"
5	..	$\frac{1.8}{100}$	..	.0018 sec.
7	...	$\frac{3.0}{100}$	..	.003 "
10	..	$\frac{4.0}{100}$	..	.004 "
14	..	$\frac{4.0}{100}$	..	.004 "
21	..	$\frac{4.0}{100}$	..	.004 "

It is interesting to note that, seven days after section (fig. 11) the value, .003 second, is approximately the same as for curarized muscle. This is in harmony with the fact that, at this stage, the peripheral part of the cut nerve is no longer excitable; after five days, on the other hand, this loss was not quite complete.

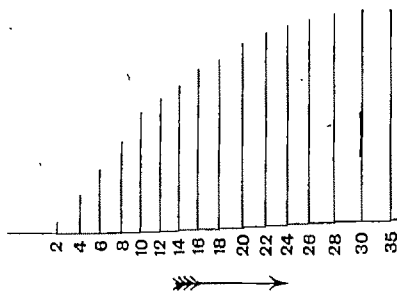


FIG. 11.—Gastrocnemius seven days after sciatic section; tracing of contractions with constant frequency of interruption (100 per second); ratio $\frac{t}{T_{100}}$, varied from $\frac{2}{100}$ to $\frac{35}{100}$. L. to R.

It seems that, from ten to twenty-one days, the value of this factor remains approximately constant. This method of examination had not been carried out in the other animals which had been allowed to survive longer—sixty-three and seventy-eight days respectively, so that information is lacking as to whether the "*limiting time*" is further increased in these cases. I had the opportunity, however, of making some observations on animals in which a motor nerve had been damaged in other ways.

Fig. 12 shows the tracing from the rectus femoris of a cat, sixty-one days after the injection of alcohol into the anterior crural nerve. It will be seen that it shows an optimum frequency of 20—a typical "*reaction of degeneration*."

In another cat the gastrocnemius was examined thirty-nine days after the sciatic nerve had been seriously damaged by being crushed with Spencer-Wells forceps. In this animal the clinical symptoms were at first like those of a complete nerve-section, but recovery was more rapid than after actual cutting of the nerve. The optimum frequency was 70, and the "limiting time" '0012 second—i.e., the condition of the muscle was functionally similar to one three days after nerve-section. Histologically (by Bielschowsky's method), the distal part of the nerve was found to be in a fairly advanced state of regeneration, showing numerous rather fine axones, without a medullary sheath, but closely associated with many "apotrophic cells" (Marinesco).

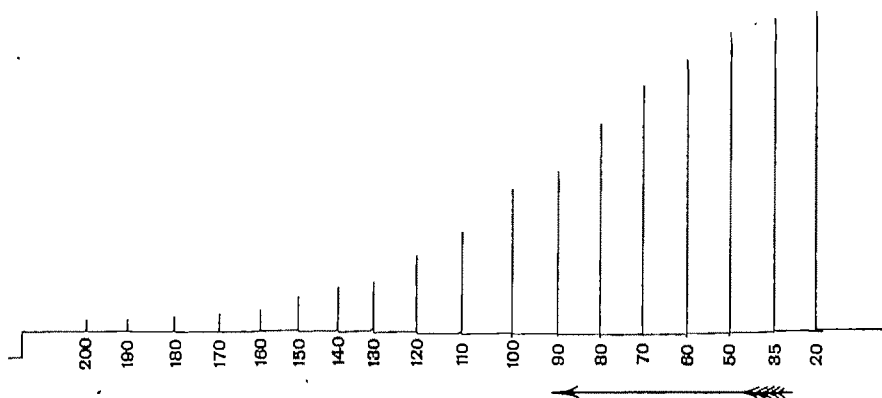


FIG. 12.—Rectus femoris of cat sixty-one days after injection of alcohol into anterior crural nerve. Tracing of contractions, with constant ratio $\frac{1}{85}$, and varying frequency of interruption, 20 to 200. R. to L.

In a third cat, the sciatic had been tightly ligatured with silk one hundred and one days before examination. This injury retards regeneration to a greater extent than simple section, owing to the fibrosis produced by the unabsorbable silk. However, the muscles were on the road to recovery, as the optimum frequency was 50, and the "limiting time" '0016 second—i.e., the muscle had returned to a functional condition about equal to that shown five days after nerve-section.

From the results here detailed, it seems then that about seven days after nerve-section the muscle behaves very like one under the influence of curare. After two or three weeks it appears to get into a fairly stable condition, which persists until regeneration begins.¹

¹ Though the functional condition appears to become stationary, the actual weight of the muscle undergoes progressive diminution for a much longer period.

V.—THE CLINICAL APPLICATION OF THE RESULTS.

The question may well be asked, "Is there any need for new methods of examining the electrical reactions of muscles, or is the present system, that of Duchenne and Erb, entirely satisfactory?" I venture to think that all those actually engaged in this work, and who are therefore in a position to appreciate its difficulties, will agree that it falls far short of practical perfection. A brief review of the method will suffice to indicate some of its defects. In the first place, the faradic current, as ordinarily employed, is quite incapable of anything approaching accurate measurement as regards any of its factors—frequency of interruption, voltage of the induced current, &c. As regards the galvanic examination, the investigator aims at measuring the least current which will just produce a contraction of the given muscle at "make," (a) when the kathode, (b) when the anode, is the stimulating electrode used. He finds in practice, however, that this is by no means easy, even in the case of any given muscle. With constant voltage, the current-strength, as indicated by the milliamperemeter, tends to be anything but constant, owing to the continually varying resistance of the circuit (due partly to the electrolytic changes in the tissues, and partly to varying contact of the electrode with the skin). Further, he has no means of knowing how much of any given current actually reaches the muscle; apart from the size of the electrode, this will be influenced by the depth of the muscle, the amount of subcutaneous fat, the texture of the skin, &c. In many text-books stress is laid on this part of the examination, from the point of view of determining whether Pflüger's Law ($K.C.C. > A.C.C.$) holds, or whether there is the "polar reversal" said to be characteristic of degenerated muscle. As a matter of fact, it is by no means constantly observed, and Wiener and Page May state that there is no real reversal, but only an apparent one, due to relative spread of the peripolar zone under these conditions.¹ The really important point to be insisted upon in the galvanic examination is the *quality* of the response—whether the normal rapid twitch is obtained, or a more sluggish contraction. In the estimation of this there is ample scope for the "personal equation," or perhaps it would be truer to say that a very large experience is necessary in order adequately to judge its character. Lastly, there is the important practical point that the galvanic examination is a painful

¹ In a recent monograph, however, E. Reiss [7] claims to have produced it under rigorous experimental conditions in frog's muscle by the action of K and NH₄ ions in suitable concentrations.

one—an especial difficulty in the case of children. The chief drawbacks, then, to this method are—the large number of unmeasured and unmeasurable factors concerned in the contractions, the difficulty of estimating the quality of the galvanic response, and the painful character of the examination.

If one judges by the enormous literature of the subject, it would seem that many investigators have been seeking a more exact method of estimating the functional condition of human muscle. Thus Zanietowski [8] has been the pioneer of a mass of work dealing with the response of muscle to condenser discharge; he and others have shown that degenerated muscle needs a higher voltage and slower discharge than does normal. In spite, however, of the many advantages claimed for this method, it has never come into anything like general use, at any rate in this country.

Mendelssohn [5] has suggested that one of the so-called "Wedensky Effects" might be turned to clinical utility. If muscle is subjected to prolonged tetanization at a given frequency and with a given strength of current, it is found that the height of contraction gradually diminishes. By suitably diminishing the frequency, the contraction can then be restored to its original height. For any given condition of a muscle, there appears to be a corresponding "optimum frequency." Mendelssohn accordingly suggests that this phenomenon might profitably be utilized for clinical purposes, but up to the present his suggestion does not appear to have been acted upon.

It is obvious that this is a special application of a principle closely analogous to that underlying the investigations described in this paper. The essential advantage of a method such as the one outlined below is, that during an investigation all the conditions remain constant except one (frequency of interruption, or ratio of make to break), which is varied in an exact, quantitative manner. *The knowledge of the muscle's condition is obtained, not by comparing its contractions with those of other muscles, but by a consideration of the variations of the actual responses of the muscle itself to known changes in the stimulus.*

At this stage I think it well to point out once more that the object of these experiments was to find data for the clinical employment of Leduc's current for muscle-testing. No meticulous accuracy is claimed for the results; for example, no attempt was made to calibrate the speed-counter attached to the interrupter, nor were steps taken to control any possible variations in the voltage of the current from the main. These defects, while perhaps sufficient to compromise the results if

claims were made to absolute mathematical exactitude, do not, in my opinion, invalidate the findings in their clinical application.

In considering how the results here detailed could best be applied for this purpose, one is faced with the question as to the practicability of applying the graphic method to man. This has been the subject of many investigations, and a large number of workers have published results obtained by various methods.¹ The most recent, as far as I am aware, is that of Larat [2]. He employs an apparatus consisting of an armlet, inextensible except in a small part of its length, which here consists of a thin india-rubber membrane. At either extremity of the membrane is a circular metal upright, joined to its fellow by a rubber bellows. This is in turn connected to an air-tambour writing on a revolving drum. The armlet is adjusted to the limb, and the muscle suitably stimulated. Any increase in girth at the level of application of the armlet stretches the thin rubber, which in turn opens the bellows and produces a fall of the tambour lever. In his book, Larat gives a large number of tracings obtained by this method. The latter, however, like the earlier ones, including the ergograph, has many obvious disadvantages. The chief of these are: (a) The more or less elaborate apparatus required, and the difficulty of satisfactory adjustment, a serious drawback for clinical work; (b) their limited applicability: while they may be fairly satisfactory for limb-muscles, none is really applicable either to the face or trunk; (c) in none of them, except perhaps the ergograph (which is of use only for the fingers or hand), is there any exact quantitative relation between the strength of the contraction and the magnitude of the lever's excursion.

For all these reasons I think that none of the present graphic methods will ever take a permanent place in routine clinical work. I have spent a good deal of time in trying Larat's and other methods, and in endeavouring to solve the problem of combining satisfactorily an electrode and recording apparatus, so that the actual contraction at the point of stimulation can be conveniently registered, but so far without much success.

It seems to me, nevertheless, that the experimental results should be capable of clinical application without the necessity of any such graphic record, however desirable the latter may be as a refinement. The testing could best be carried out as follows:—

Begin with the ratio make : total period at 10 : 100, and frequency of interruption 100. Adjust the strength of current till a contraction

¹ For list of these, see Mendelssohn's article in *Boruttav's Handbuch* [5].

is just obtained. Now, keeping everything else constant, diminish the frequency to 20 or 25. Normal muscle should no longer give a contraction, but degenerated muscle will give a much better one. Alter the frequency gradually from 20 to 200, and decide as far as possible which is the optimum. Or, better, keep the frequency constant at 100, and vary the contact-ratio (x). For normal muscle, the size of the contractions should be independent of the value of x between the limits 5 and 50. For degenerated muscle, the size of the contractions should increase as x increases, until an optimum is obtained. The lowest value of x for an optimum contraction could be taken as an index of the condition of the muscle. What one really determines in such an observation is the duration of stimulus above which "accommodation" comes into full play (*v.s. p.* 278),—i.e., a time which has been shown to vary definitely according to the functional condition of the muscle.

I am at present engaged in collecting material for examination on these lines. The facilities for such work are unfortunately scanty, as the apparatus is fixed in an experimental laboratory, a situation not very suitable for clinical investigations. I hope, however, in a subsequent paper to publish a full account of the clinical findings, when sufficient material has been examined.

This much can be confidently stated at the present time, that Leduc's current is far less painful than those usually employed in muscle-testing.

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PUBLICATIONS RECENTLY RECEIVED.

[Notes on a book under this heading do not preclude a subsequent review.]

La Maladie de Little, Étude Anatomique et Pathologique. Par Mme. LONG-LANDRY. Pp. 147. Paris: Delarue, 1911.

It cannot be denied, as the authoress states, that in relation to its frequency there is probably no disease of the nervous system about the pathology of which less is definitely known than that large group of congenital spastic paresis included in Little's disease. The relatively small number of cases in which a complete and satisfactory pathological examination has been made, and the long period after the onset of the primary disease at which they have come to examination, is probably the explanation.

This thesis is based on the examination of four cases; in three the most important change was a diffuse meningo-encephalitis, associated with more or less intense inflammatory changes in the ependyma and the choroid plexus, while in the fourth the primary disease was chiefly spinal, and took the form of a diffuse meningomyelitis. There may be many and various causal factors, but the site of the primary lesion, the stage of development at which it occurs, and the permanent effects it produces are recognized as being more important in determining the symptoms than the nature of the disease process. The two large groups of causes are, however, the infective, which are pre-natal, and the traumatic, which occur during birth. Syphilis, and perhaps tubercle, are the chief infective agents. Premature birth, however, seems to be often a determining factor.

Le Corps Calleux—Étude Anatomique, Physiologique et Clinique. Par J. LÉVY-VALENSI. Pp. 216. Paris: Steinheil, 1910.

These anatomical and physiological conclusions are drawn from a relatively small number of experiments, in which the corpus callosum was either cut or excited by a faradic current, and the clinical material is limited to two personally observed cases. The records of many other cases are, however, collected from the literature.

The author's chief conclusions are that the callosal fibres connect non-symmetrical portions of the hemispheres; none of them enter the external capsule as has been stated, but possibly some pass to the posterior limb of the internal capsule. The tapetum also receives a considerable contribution from them.

Section of the corpus callosum produces no symptoms in monkeys, but dogs become dull, awkward in certain movements and seem to forget acts they have learned. Human beings with lesions of the corpus callosum do not present any pathognomonic features, but the motor disturbances are often bilateral and the mental symptoms to which Raymond has drawn attention—a change in character, loss of association of ideas, and a disturbance of memory for recent events—are often significant. Left-sided apraxia is, however, the most important sign. One chapter of the monograph is devoted to an analysis of apraxia.

The Goulstonian Lectures on the Sensibility of the Alimentary Canal.

By ARTHUR F. HERTZ, M.A., M.D. Pp. 83. London: Frowde, Hodder and Stoughton, 1911.

This book contains the lectures delivered before the Royal College of Physicians in March, 1911. The various forms of sensibility are considered in order, and the author concludes that all viscera are insensitive to tactile stimuli, and that heat and cold can be appreciated in the œsophagus and anal canal only. On the other hand the stomach and the intestines are sensitive to stimulation with alcohol but not with dilute mineral and organic acids. The sensations of fulness and distension, emptiness and hunger are dealt with at length. Nearly half the book is devoted to a full consideration of various forms of pain, and the author concludes that tension is the only cause of true visceral pain, which may be referred or may be situated in the region of the affected parts.

Vorlesungen über den Bau der Nervösen Zentralorgane des Menschen und der Tiere. Von Professor Dr. LUDWIG EDINGER. Erste Band. Das Zentralnervensystem des Menschen und der Säugetiere. Achte umgearbeitete und sehr vermehrte Auflage mit 398 Abbildungen und 2 Tafeln. S. 530. Leipzig: Vogel, 1911.

This admirable work has been revised once more by the author, and the figures and diagrams are even more excellent than in the preceding editions. The text is a model of clarity, and the illustrations so wisely chosen that every difficult point is explained by an original figure, which gives exactly the information required. No neurologist can afford to be without this book.

Die Pupillenstörungen bei Geistes- und Nerven-krankheiten (Physiologie und Pathologie der Irisbewegungen). Von Professor O. BUMKE. Zweite vollständig umgearbeitete Auflage. S. 357. Jena: Gustav Fischer, 1911.

The second edition of Bumke's book, which has appeared after an interval of six years, is considerably enlarged. All the recent anatomical and physio-

logical work on the nervous control of the pupillary movements and reactions is dealt with in the first two chapters. In the third chapter the general pathology of the iris movements is discussed, and the fourth deals with the pupillary anomalies in organic and toxic diseases of the nervous system, and in certain neuroses and psychoses. The methods of examining the pupils are fully described in an appendix. The book also contains a very complete bibliography on the subject, and a useful index.

A Textbook of Experimental Psychology, with Laboratory Exercises.

By CHARLES S. MYERS, M.D., Sc.D. Second Edition. Part I: Textbook, pp. 344. Part II: Laboratory Exercises, pp. 107. Cambridge: University Press, 1911.

This excellent textbook has been greatly improved in the second edition. It is still characterized by clear and concise exposition, but much new material has been added and almost every chapter has been re-written. Separation of the text from the laboratory exercises enables the student to read the general statement whilst consulting the description of the experiments upon which it is founded.

Unsoundness of Mind. By T. S. CLOUSTON, M.D., LL.D. Pp. 360. London: Methuen, 1911.

This book is an attempt to explain "unsoundness of mind" in terms comprehensible by the "intelligent layman." The author disarms criticism by this preliminary statement of the objects in view and then proceeds to consider mental disorders as disturbance of brain-function. Chapters are devoted to heredity, to brain-poisons and to the predisposing causes of insanity. Mania, melancholia and the circular psychoses are dealt with shortly; the mental defects of the climacteric and old age are touched upon, and the organic insanities described in simple language. Then follow chapters on crime, education, and the hygiene of mind.

Compendium of Regional Diagnosis in Affections of the Brain and Spinal Cord. By ROBERT BING. Translated by F. S. Arnold, B.A., M.B., with 70 illustrations. Pp. 215. London: Rebman. No date.

This is a useful compendium for the student and general physician to whom the complexities of the anatomy of the nervous system are not familiar. The diagnostic results of most of modern work on the cerebrum, cerebellum and brain-stem are included, and good diagrams are given to illustrate each syndrome. But it is a pity that the descriptions on these figures have been left in the original German, which will be unfamiliar to many for whom this translation is intended. It is a practical guide and makes no pretence to deal with scientific principles.

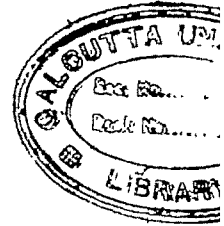
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EDITOR.

[MARCH, 1912.]



BRAIN.

PART IV., VOL. 34.

Original Articles and Clinical Cases.

PROGRESSIVE LENTICULAR DEGENERATION: A FAMILIAL NERVOUS DISEASE ASSOCIATED WITH CIRRHOSIS OF THE LIVER.¹

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¹ This paper formed part of a thesis for the degree of M.D. of the University of Edinburgh, July, 1911, for which a gold medal was awarded.

pyramidal motor disease, the importance of which is apparent not only because of its rarity, but also by reason of the light it sheds on such diseases as *paralysis agitans*.

The pathology of the disease is as striking as the clinical syndrome. As a glance at the figures will show, the lesion is a *bilateral symmetrical softening in the lenticular nucleus*, involving more particularly the putamen; the globus pallidus is affected to a less extent. In addition the external capsule may be partly included in the area of disease; the caudate nucleus may be slightly degenerated, but—most important of all—in a pure case the internal capsule is absolutely intact. The optic thalamus similarly escapes. Certain important secondary degenerations follow from the lenticular disease. If the diseased areas are examined minutely it will be found that a change begins apparently round the lenticulo-striate vessels, as a result of which the substance of the lenticular nucleus begins to shrink and atrophy; its cells and its fibres disappear, and their place is taken by glial tissue, the laminæ medullares and internuncial fibres becoming less and less distinguishable; in advanced cases the nucleus breaks down entirely, and a cavity formation is the result. There is no sign of syphilitic disease of the vessels concerned, all of which are patent; their walls, indeed, often appear to be rather thinned. Gross vascular disease is conspicuous by its absence. It is clear the condition is not due to a thrombotic process in the distribution of a particular blood-vessel; on the contrary, the peculiar selective action of the morbid agent will be readily appreciated when it is remembered that the lenticular nucleus is supplied from three different sources. Yet in this disease one collection of grey matter is singled out, while neighbouring grey matter areas are left intact. Compared with this bilateral symmetrical degeneration of the lenticular nucleus and associated alterations, the other changes found in the central nervous system are slight and comparatively unimportant; they will, however, be duly recorded in their place.

What must be considered, as it seems to me, the most curious and the most remarkable feature of this familial nervous disease is the constant presence of a profound degree of *cirrhosis of the liver*. This hepatic cirrhosis does not reveal itself by any symptoms during life, nevertheless it is always found after death. It is mixed in type, as will be subsequently shown. Syphilis and alcohol, as possible morbid agents in connexion with this cirrhosis, can, I believe, be entirely excluded. This association, in young people, of cirrhosis of

the liver with bilateral symmetrical softening of the lenticular nucleus constitutes the disease from the pathological standpoint; clinically, the symptoms are exclusively nervous. Other organs (thyroid, &c.) show changes of secondary importance, to be described below.

Progressive lenticular degeneration, as the disease may be called, is not one with which the medical profession is familiar. As far as I can discover, no case has been recorded since 1890, with the very doubtful exception of one reported by Anton, of Halle, under the title of "Dementia Choreo-asthenica, with Juvenile Nodular Cirrhosis of the Liver," some three years ago. In all probability this case was one of congenital syphilis. The total number of cases of the disease that have been published amounts to six only. Of these, two (brother and sister) were reported by Gowers in 1888 under the name of "Tetanoid Chorea, associated with Cirrhosis of the Liver"; one by Ormerod in 1890; three (two brothers and a sister) by Homén, of Helsingfors, also in 1890.

Ormerod called his paper "Case of Cirrhosis of the Liver in a Boy, with Obscure and Fatal Nervous Symptoms." Homén described the condition as "A Peculiar Disease occurring in Three Members of a Family in the form of a Progressive Dementia, probably Lues hereditaria tarda." All these six cases were fatal. In Gowers's cases (both acute) no lesion of the central nervous system was found. In Ormerod's case (acute) there was slight bilateral symmetrical softening in the putamen. In Homén's cases (all chronic) the same symmetrical lenticular lesions were found in all three, together with sundry other changes to be referred to later. All six had marked cirrhosis of the liver.

Since 1890 there has been no further light thrown on the mystery of the disease, nor has there been any adequate pathological investigation, so that the subject has remained a *terra incognita*.

In this paper will be described four cases of the affection which have been personally observed and diagnosed (in all but one the diagnosis was made during life), in three of which it has been possible to make a *post-mortem* examination.

The first patient (S. T.) came under observation in 1905, and died on July 28, 1908. At the autopsy bilateral degeneration of the lenticular nucleus was found, coupled with cirrhosis of the liver.

The second patient (D. P.) came under observation in 1906, and died on March 3, 1907. Here, also, cirrhosis of the liver and a slighter degree of lenticular change were discovered.

The third patient (E. P.), a brother of the above, came under notice

in 1907. This patient was exhaustively examined in the summer of 1910. He died on September 20, 1910, and in his case identical findings were obtained at the autopsy.

The fourth patient (M. To.) came under observation in the autumn of 1911, and at the time of writing she is still living.

In addition to these four personal cases the record of two other cases of the disease has been obtained, one of which occurred in the family described by Gowers, but has not hitherto been published, as the notes were lost years ago. By a piece of good fortune I was able to trace the mother of the family, an old lady aged 70, and to obtain from her the clinical details of this new case. The other is one referred to by Ormerod in his paper of 1890; the notes, not hitherto published, are preserved in the National Hospital, Queen Square.

Thus I am in a position to add no less than six cases to the existing record, scanty as it is; and a consideration of their remarkable clinical and pathological features may help to elucidate the nature of a rare disease, which presents problems that interest the clinician, the pathologist, and the physiologist. The application of modern methods of investigation to the material at my disposal, it may be hoped, will serve to remove some misconceptions as to the nature of the affection, and to establish as a morbid entity this "progressive lenticular degeneration," on which much work yet remains to be done.

It is my pleasant duty here to acknowledge my deep indebtedness to many who have aided me in this research, which has extended over six years. My grateful thanks are due to Sir William Gowers, Sir David Ferrier, Dr. J. A. Ormerod, and Dr. H. H. Tooth for permission to utilize their notes on the cases that have been at one time or another under their care in the National Hospital, and for encouragement and suggestions in the prosecution of the work; as also to Sir Victor Horsley; Dr. James Taylor, and Dr. Holmes, of the National Hospital; Dr. W. H. B. Stoddart, of Bethlem Royal Hospital; Dr. Parkes Weber; Dr. Thomas Wilson, of Birmingham; Dr. Max Tylor, of Wisbech; Dr. W. D. Moore and Dr. G. W. Smith, of Virginia Water Sanatorium; Dr. T. R. Elliott and Dr. Otto May, of University College Hospital; Dr. F. W. Goodbody, of University College; Dr. Yunge-Bateman, of Folkestone; and Dr. Reymond, of the Sanatorium, Chexbres, Switzerland, for invaluable assistance at various times. Further, I cannot refrain from acknowledging here the extent to which my task has been lightened by the willing co-operation of different members of the families concerned, who, by their intelligent interest in a subject which cannot but have

painful memories for them, have rendered me services for which I am profoundly indebted to them.

CHAPTER I.—HISTORICAL.

THE first two recorded cases of the disease which forms the subject of this monograph we owe to the clinical acumen of Gowers, who, in the year 1888, published in his well-known "Manual" the following paragraph, under the title "Tetanoid Chorea" (vol. ii, p. 656):—

"A case was recently under my care that presented symptoms intermediate between those of chorea and tetany. The disease was fatal, and no lesion was found after death. The patient was a boy, aged 10. A brother was said to have died from some affection similar to that from which this child was suffering.¹ There was a history of three other relations having suffered from maladies resembling chorea. In this patient the disease commenced gradually seven months before death. The symptoms consisted of tonic spasm, which was continuous, and varied by paroxysmal attacks of similar but more intense spasm. The face was involved on both sides, so as to cause a constant peculiar smile. The tongue was pressed back against the palate in such a manner as to impede swallowing and prevent speech. The arms were extended, pronated, and rotated inwards, so as to bring the back of the forearms outwards, while the fingers were generally slightly flexed at all joints, but at times were extended and slowly moved in the irregular way characteristic of athetosis. The legs were extended at all the joints, the feet being over-extended in talipes equino-varus, and the toes were flexed. At times the spasm at the hip became flexor, so that the extended legs were raised off the bed. The muscles of the trunk were also involved in the spasm. At first the left side was the more severely affected, but afterwards the spasm became equal on the two sides. The electric irritability of the muscles was normal, and there was no mechanical excitability of the nerves. There was considerable pyrexia during the more severe stage of the disease. The boy steadily emaciated, and died from exhaustion. The whole central nervous system appeared normal to the naked eye, and no distinct morbid appearances could be discovered on microscopical examination. I have not been able to find a description of any similar case."

¹ See footnote, p. 301.

This bare outline of an historic case, as the earliest recorded instance of a new disease must always be, leaves some points unnoticed: the fact that the boy was found to have cirrhosis of the liver is not mentioned, as its significance was not at that time appreciated. The original notes, however, preserved in the National Hospital, Queen Square, are remarkable for their fulness and accuracy of description, and in particular for the wealth of illustration incorporated with them. Copies of the drawings and old silver prints, with which the notes are enriched, will be found below.

Not long after, the sister of Case 1, a girl of 15, came under the care of Gowers, suffering from identical symptoms, which ran an identical course, and terminated fatally in a few months. Realizing the great interest of the condition, that observer republished the cases in the *Review of Neurology and Psychiatry* for 1906, in fuller detail, under the heading "Tetanoid Chorea, and its Association with Cirrhosis of the Liver." In the opening paragraph of this communication the following passage occurs:—

"These cases were under observation many years ago, and their record has been waiting for other facts that might elucidate their mystery, but waiting in vain. They are now presented in the hope they may direct further attention to these strange forms of disease."

From the original notes of these two cases the following précis has been made, in which the cardinal features of the condition, as observed by Gowers, are succinctly described from the clinical and pathological standpoints.

(The full notes of the cases will be found in the Appendix, p. 489.)

Case 1.—Sydney M., aged 10, was admitted to the National Hospital, Queen Square, London, on October 5, 1886, under the care of Sir William Gowers.

The patient was the eighth of fourteen children, and had had no illnesses except typhoid fever at the age of 3. An uncle on the father's side was said to have been affected in the same way as the patient, and to have recovered after an illness of twelve months. The eldest brother had died at the age of 15 of some form of paralysis.¹

The symptoms began gradually, without exciting cause, three months before the patient was admitted to the hospital, with clumsiness and awkwardness of the hands; about the same time involuntary movements of the arms and legs commenced. On admission constant slowly changing movements in the limbs

¹ This is the case whose notes have been lost, but whose history has been obtained from the mother of the family, still living at the age of 70. It will be found below among the new cases (my Case 5, p. 361). There is no doubt it belongs to the series.—S. A. K. W.

attracted attention, as well as a generalized spasticity. A contraction of the zygomatics caused a continuous smile, now greater on one side, now on the other. The mouth was usually held spasmodically open, and the tongue generally back in the mouth; occasionally it was slowly protruded. When told to shut his mouth the patient used to push the lower jaw up with his hand, then the spasm of the muscles would seem to give way and he would close his mouth easily, but it returned to the widely open position in a minute



FIG. 1.—S. M. (Gowers.) The tremors, spasticity, contractures, &c., are well seen. From one of the original silver prints (dated 1886), kindly lent to me by Dr. Thomas Wilson.

or so. A great degree of dysphagia was present, and also of dysarthria; speech was usually almost unintelligible, but occasionally the patient could utter words or sentences more distinctly, especially in the morning. As he lay in bed he often made a low whining sound.

The muscles of the neck, trunk, and limbs were all involved, in varying degree, in the generalized tonic spasm; sometimes involuntary movements, not unlike athetosis, occurred in the fingers; at other times the arms and hands were definitely tremulous. The extremities were in a state of contracture, the



FIG. 2.—S. M. (Gowers.) Note the apparent indifference of the patient to the fact that his mouth is widely open. From the original in the notes at the National Hospital.

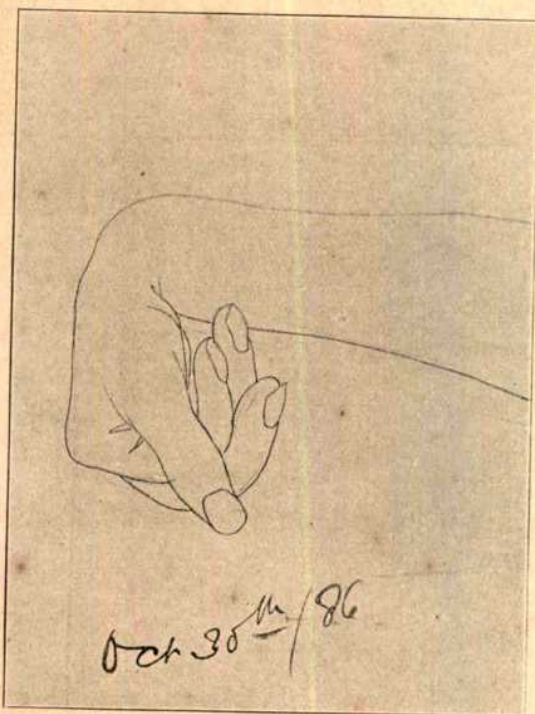


FIG. 3.—S. M. (Gowers.) From the original drawing in the notes of the case at the National Hospital.

fingers flexed, and the forearms pronated, while the feet were extended and inverted, and the toes flexed; in spite of the great degree of spasticity, occasionally it relaxed sufficiently to allow the contractures to be overcome.

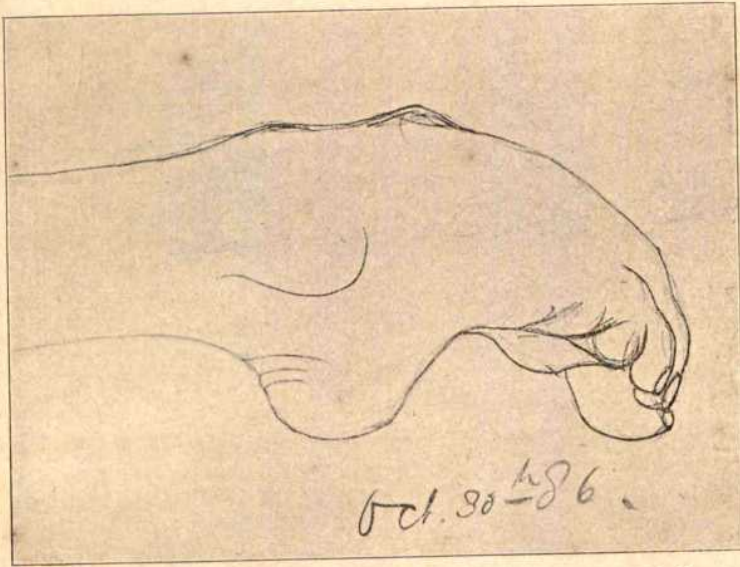


FIG. 4.—S. M. (Gowers.) From the original drawing in the notes of the case at the National Hospital.

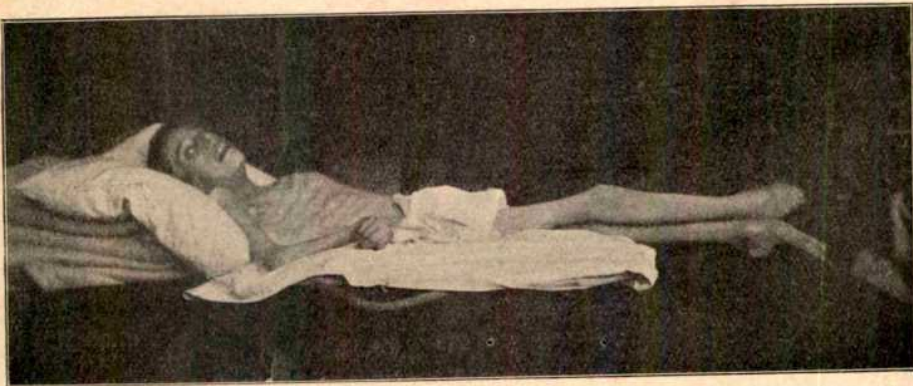


FIG. 5.—S. M. (Gowers.) Photograph taken shortly before death, showing spastic smile, contractures, and profound emaciation. From the original silver print (dated 1886), kindly lent to me by Dr. Thomas Wilson.

Voluntary movement was interfered with by the spasm to a less extent than might be anticipated; the patient could take hold of any object with little difficulty. He was able to walk, although the heels were usually off the ground, but sometimes they came down and he walked naturally. There was

no sphincter impairment. The knee-jerks were present; ankle-clonus was not obtained. The plantar reflex was noted as "slight." (This was long before the days of insight into the significance of the plantar reflex.) The cremasteric reflex was active; the abdominal was not elicited. Sensation was everywhere

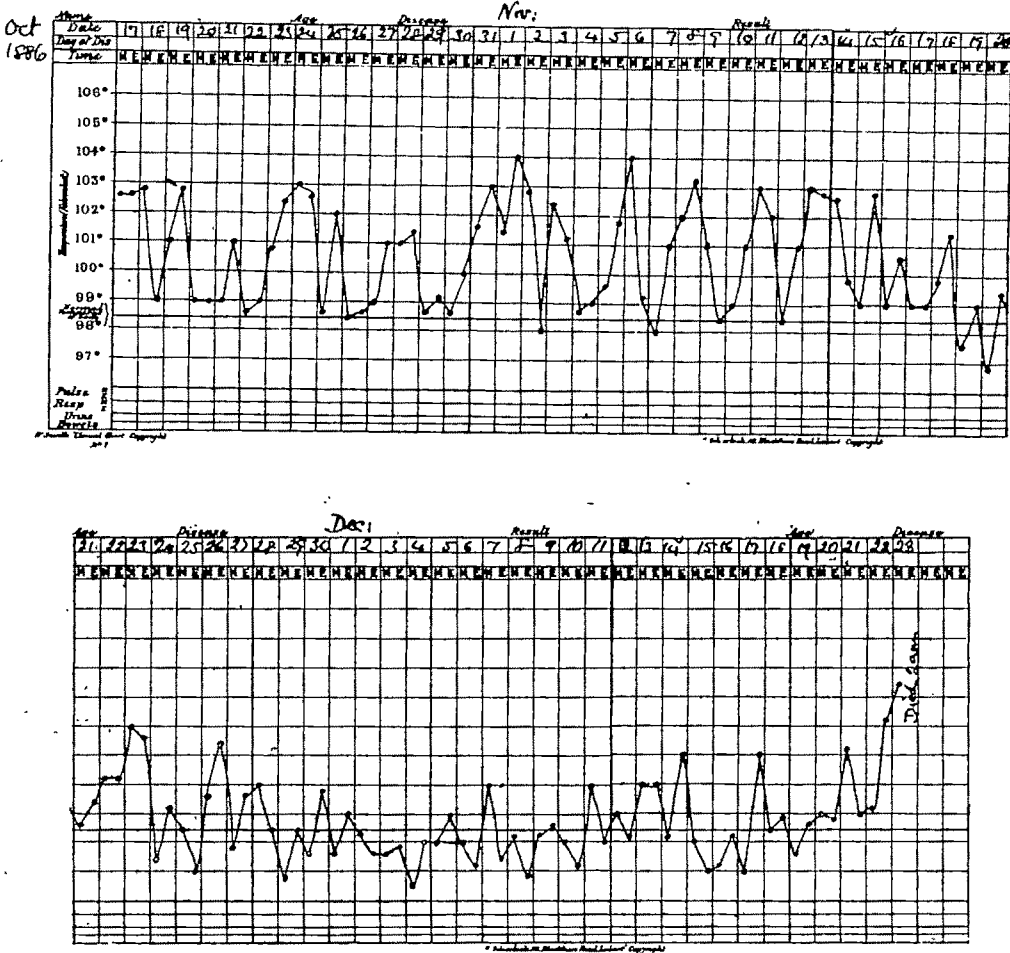


FIG. 6.—Temperature chart of S. M. (Gowers.)

normal. The optic discs were normal; the mind was clear; the patient could write down what he was unable to articulate, and evidently understood everything that was said to him.

During the first few days after admission some improvement occurred, but thereafter the patient became steadily worse. His temperature rose, and continued highly irregular (fig. 6). He became drowsy, and began to pass his urine

and stools into the bed. The dysarthria and dysphagia increased; the spasmodic contractions of the musculature became intensified; the extremities became more definitely contracted. Emaciation set in rather rapidly, and the patient gradually sank into a more and more helpless state, with the result that eleven weeks from the date of his admission, and six months from the beginning of the symptoms, he died.

A *post-mortem* examination was made. Naked-eye investigation of the brain, cord, and membranes revealed nothing abnormal. The liver was noted to be firm, hard, and lobular, and was evidently cirrhotic. Portions of the cortex, cord, peripheral nerves and muscles, examined microscopically, did not show any departure from the normal.

A glance at figs. 1 to 5, which have been reproduced partly from the photographs in the notes and partly from original silver prints, kindly lent to me by Dr. Thomas Wilson, of the General Hospital, Birmingham, who was Resident Medical Officer to the National Hospital at the time, will serve admirably to take the place of fuller description. It must be remembered they were taken before the days of instantaneous photography, hence the tremulous movements of the arms are well shown; indeed, for my purpose, this is almost to be preferred, as it accentuates the contrast between the spastic smile and wide-opened mouth and the tremors of the upper limbs. The contractures of the hands and feet are well seen. The progressive emaciation can be readily appreciated. The drawings are copied from the original sketches in the notes, depicting the condition of the distal portions of the limbs.

No one who compares these photographs of twenty-five years ago with the series illustrating my own cases can fail to be struck by the very close resemblance between them. The same spastic smile, open mouth, tremors, contractures, and emotionalism, are portrayed by the unerring camera in such a fashion as to render comment needless.

In the light of subsequent knowledge the points to emphasize in Sydney M.'s case are the following:—

A boy, aged 10, suffers from an acute and fatal illness of six months' duration, whose features suggest strongly it is of a toxic or toxo-infective nature. The only certain pathological condition found *post-mortem* is cirrhosis of the liver. Nevertheless the clinical symptoms are exclusively nervous and are from the outset severe and progressive. They consist of dysarthria and dysphagia, emotionalism, generalized rigidity of the musculature of face, trunk, and extremities, tremulous and sometimes irregular involuntary movements of the limbs, without any true paralysis, as most ordinary movements can be performed,

contractures that can at first be overcome, but gradually establish themselves permanently, and emaciation. Sensibility is intact, and there is no definite indication of direct interference with the pyramidal system.

Case 2.—Charlotte M., aged 15, the sister of Sydney M., was admitted to the National Hospital on August 29, 1888, under the care of Sir William Gowers.

She had always been a healthy girl. Menstruation began about a year before, and was quite regular for seven months, then ceased abruptly.

For the last nine months she had become listless and lethargic, and

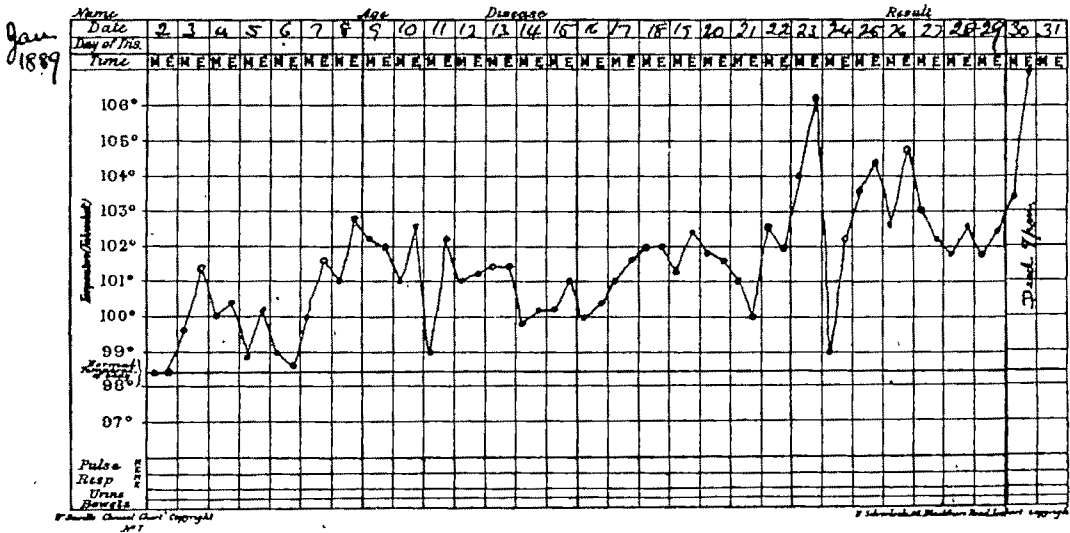


FIG. 7.—Temperature chart of C. M. (Gowers.)

disinclined to do anything. Her speech was noticed to become thick and indistinct, and occasionally saliva escaped from her mouth. On admission she was seen to be a heavy-looking girl, with mouth generally open and lower lip hanging down, and she was easily excited to laughter. Her tongue was found to be tremulous. She presented no other sign, and no evidence of organic disease of the central nervous system. Accordingly she was discharged after six weeks, but a month or two later involuntary movements of the limbs began, and progressed steadily, so that she was "always on the work." She used to be able to write well, but her writing rapidly deteriorated, and became almost illegible. She was readmitted to the hospital on January 2, 1889. On examination the striking feature was the more or less constant rhythmical tremor of arms and legs. As she lay in bed there was constant

regular movement of the feet with alternating contractions of flexor and extensor movements at the hips and knees. Similar rhythmical movements, consisting of alternating contractions of flexors and extensors, occurred in the arms. They could occasionally be stopped for a few seconds by voluntary effort. The lower extremities were rigid and in a state of contracture, and passive movements caused some pain.

The illness ran a steadily downhill course. The patient became emaciated, and fever developed (fig. 7); the tremors persisted, the rigidity increased. No sign of organic nervous disease was present, in the ordinary sense, except that the knee-jerks could not be elicited, presumably because of the rigidity. Death took place on January 30, 1889.

On pathological examination no definite morbid appearance was found in the brain or cord, but the liver showed an advanced degree of cirrhosis, strands of connective tissue enclosing nodules of varying size.

Both from the clinical and the pathological aspect the resemblances between this case and the previous one are of the closest. In spite of the grave and progressive nature of the nervous symptoms, no obvious lesion was found in the brain or cord to account for them, whereas an entirely latent and unsuspected hepatic cirrhosis was discovered. It is a curious feature of the disease that in all the recorded instances, as well as in my own series, with one exception (my Case 6), this cirrhosis has not revealed itself by any of the usual signs. Of this second case it may be remarked that the involuntary movements were definitely rhythmical and tremulous, more so than in the first case. It will be seen later that on this point the resemblance to the cases of the disease reported here for the first time is perfect. Although Gowers has described these cases as "tetanoid chorea," the involuntary movements were not constantly choreiform in the first case and apparently not at all in the second; while the epithet tetanoid is intended to specify a clinical appearance solely and not a pathological relationship.

The third case was recorded by Ormerod in the *St. Bartholomew's Hospital Reports* for 1890. The clinical notes were made without any knowledge of the above National Hospital cases; the resemblances, therefore, are all the more striking. The résumé of his case, given by Ormerod in the opening paragraphs of his paper, is here quoted in its entirety:—

Case 3.—"A boy, aged 10, previously healthy, is admitted with the following history. He has been getting ill gradually for three or four months. The

symptoms alleged are, in order of their development, weakness of right hand and arm, with cramped position of the fingers, soon followed by difficulty of speech. 'Drawing' of the face, then an unnatural gait. Speech gets worse; he seems 'silly'; has some difficulty in swallowing. Gait gets much worse. Lastly, some affection of left arm and hand.

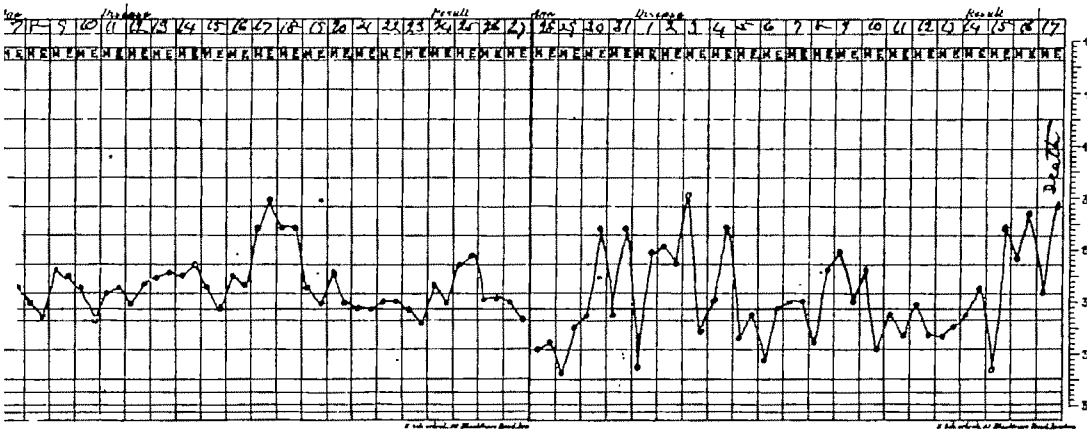
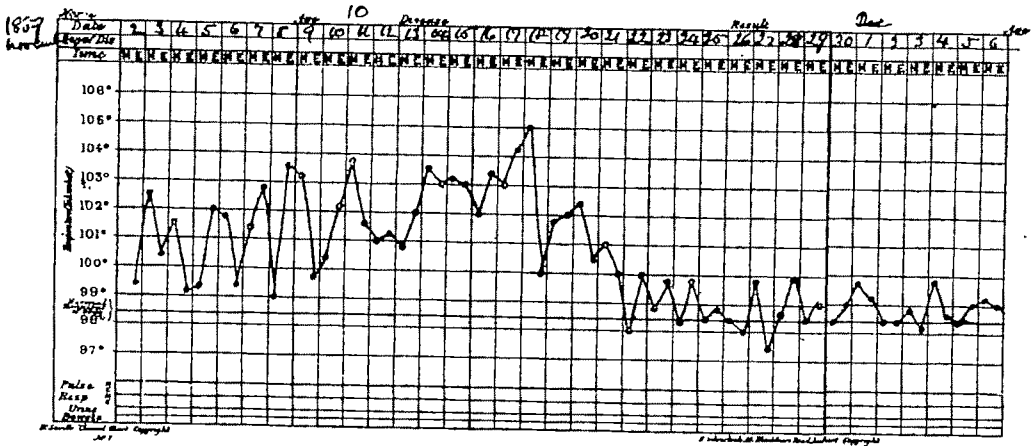


FIG. 8.—Temperature chart of W. S. (Ormerod.)

"The existence of these symptoms is verified after admission—a clumsiness of the right hand, with flexion of the thumb into the palm, and a tendency to rigidity at the knees, with uncertain, stiff gait, are noted. The only marked symptom, however, is inability to speak. He is not aphonic; he understands

all that is said to him, but says nothing, except on some rare occasions, when he speaks quite intelligibly. He has difficulty in protruding his tongue.

"In about three weeks paroxysms of pain, with contractions, begin in the left hand; he takes to shrieking. In ten days more he becomes very noisy, and apparently idiotic. The facial spasm becomes more marked. Nevertheless his symptoms are so vague, and apparently so much under his own control, that it seems probable that there is no organic lesion to account for them.

"This view, however, is negatived by the advent of more serious events; for, six or seven weeks from the time of admission, he becomes feverish (fig. 8); pulse very frequent; profuse sweatings. The legs become permanently drawn up, the right hand becomes weak. and like the left.

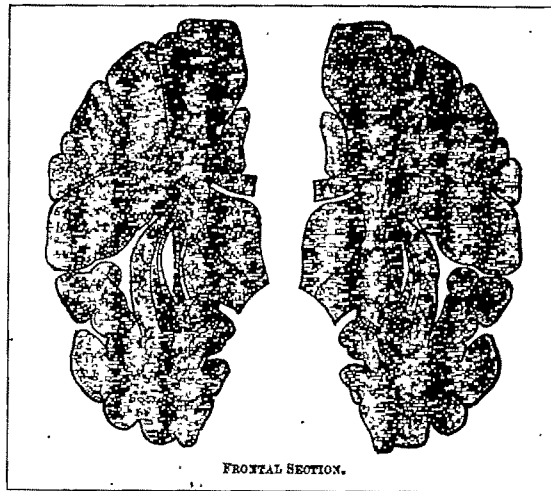


FIG. 9.—W. S. (Ormerod.) Bilateral softening in the putamen. (From *St. Bartholomew's Hospital Reports*, 1890.)

"His mental condition appears to get worse, and he lies howling all the day long. Finally, an acute bed-sore and signs of cystitis appear. In spite of a certain temporary remission, his condition gets worse, and the poor child dies, miserably emaciated, and his limbs distorted by contracture. Death takes place about four months from the time of his admission, and some seven or eight months from the commencement of his symptoms.

"*Post-mortem*, certain slight changes are found in the nervous system, but he has well-marked atrophic cirrhosis of the liver."

These changes in the nervous system are, as a matter of fact, of great importance. They consisted in a bilateral and symmetrical

area of softening, occupying the putamen or outer section of the lenticular nucleus, extending for about an inch in an antero-posterior direction, and involving chiefly its external part. The tract of disease on the right side was smaller in extent than that on the left. Fig. 9 is a reproduction of the drawing given in Ormerod's paper, and shows the appearances on frontal section at the level of the optic commissure. Microscopically in the affected areas were found closely packed lymphoid cells, in which a few vessels ran; the changes are supposed by the author to have been inflammatory. The spinal cord was perfectly normal. In the liver the characteristic appearances of cirrhosis were present, although the cells of the lobules were less degenerated than might have been expected, while amid the connective tissue growth bile-ducts were very numerous, and very prominent objects.

No one who peruses this brief sketch of these three cases, now more than twenty years old, can fail to appreciate their evident similarity. Indeed, they form a special group by themselves, for the cases published by Homén, as well as those of my own series, are, on the whole, more chronic and more slowly progressive. While, however, the latter may be in a sense less dramatic, yet they were none the less fatal, and their pathology is identical with that of the case that has just been described. These first three cases occurred in young people, beginning in an insidious way without apparent cause, and they were characterized by dysarthria, dysphagia, hypertonicity of the musculature, involuntary spasmodic movements, sometimes slow and tonic, oftener clonic and tremulous, contractures, and emaciation. The patients were obviously ill, with high, irregular fever, and great helplessness and weakness, yet both Ormerod and Gowers were struck by the fact of the occasional variability of the symptoms, and pointed out how readily and reasonably they might have been regarded, at least to begin with, as "functional"—i.e., hysterical. There was a curious disproportion between the clinical appearances and the actual objective signs of organic nervous disease. It may be remarked in this connexion that two of my own cases were at one time thought to be hysterical, and treated accordingly. Our ignorance of the symptomatology of extrapyramidal motor affections, I believe, is the explanation of mistakes of this sort. Few doubt to-day that paralysis agitans is an organic disease of the nervous system, yet not so long ago its accepted place in the text-books was with neurasthenia and hysteria.

Before passing on to the next group—viz., those described by Homén

—it may be noted that Ormerod specifically draws attention to the following three points:—

- (1) The presence of a cirrhotic liver in so young a subject.
- (2) The absence during life of all ordinary symptoms of cirrhosis of the liver.
- (3) The presence of severe and fatal nervous symptoms in a case where the nervous lesions found *post-mortem* were comparatively insignificant.

These problems can be better discussed after consideration of the results of the pathological investigations described farther on, which will materially aid us in this respect. There need be no occasion for embarrassment at the apparent absence of any definite positive findings in the brain in Gowers's cases, for in the first place the acute nature of the malady may not have allowed time for the development of changes that could be recognized, and in the second place histological technique has made considerable strides since the eighties of last century.

Under the title of "Eine eigenthümliche bei drei Geschwistern auftretende typische Krankheit unter der Form einer progressiven Dementia, in Verbindung mit ausgedehnten Gefäßveränderungen (wohl Lues hereditaria tarda)," Homén, of Helsingfors, in Finland, published in the *Neurologisches Centralblatt* for 1890, the same year as Ormerod's paper appeared, and again more fully in the *Archiv für Psychiatrie* for 1892, an account of an apparently unique and unknown familial disease, which for various reasons, but in spite of the lack of positive evidence, he concluded might be a delayed manifestation of hereditary syphilis, a disease in which a sister and two brothers out of a family of eleven were affected, which ran a steady progressive course, and in each instance ended fatally. Its duration in these cases was three and a half, six, and seven years respectively. The clinical picture presented by the disease, and the pathological changes found *post-mortem* were not only identical in all three, but on all essential points offer the closest analogies to the description already furnished of the English group.

The following résumé of the cases is made from Homén's second paper [6], and includes the main features of this remarkable familial affection.

Case 4 (Homén's No. 2).—Alfred K. was born in December, 1866, and was in perfect health up to the age of 20. Without any apparent reason

he then began to suffer from a general listlessness and loss of appetite, and at the same time he seemed to become slow in his mental processes, and, generally speaking, more "simple." After about six months his gait was noticed to be stiff and uncertain; his articulation became indistinct, and tremor appeared in the arms and hands and became more and more pronounced. The stiffness, dysarthria, and tremor advanced to such a degree that the patient was ere long reduced to a state of helplessness.

On admission to hospital the chief symptoms and signs were as follows:—

The youth had a rather childish and stupid expression, the facial muscles being fixed and stiff; he seemed to understand everything that was said to him, but he scarcely ever spoke, and then always slowly; there was slight difficulty in moving the tongue. As he lay in bed the head was seen to have a more or less constant to-and-fro movement; the mouth was almost always open, the lower jaw tremulous; both arms and hands were in a state of contracture, the former being somewhat flexed at the elbows and the fingers flexed proximally but extended distally; they were very stiff, and passive movements were with difficulty impressed on them. The right hand was less affected than the left. A slow slight tremor of the hands from the wrists, in a radio-ulnar direction, was constantly observable, though occasionally it was more rotatory; a rhythmical tremor of alternating flexion and extension was often noticeable at the elbow. The lower extremities were also in a condition of contracture, and when the patient was put on his feet he required strong support. Even then the rigidity made progression almost impossible. Tremor of the legs was frequently noticed, especially when any voluntary movement was executed, chiefly consisting of alternating flexion and extension at knee and ankle. Voluntary effort always aggravated the tremor of the arms. There was some wasting of the muscles; sensibility was intact.

The patient's condition became steadily worse. Occasionally he spoke a few words distinctly, but gradually he became more and more inarticulate, as a rule simply giving vent to unintelligible sounds. The contractures increased, the tremors became generalized, and were sometimes observed in "attacks" which lasted for five or ten minutes and involved the whole musculature. Saliva escaped from the opened mouth. Attacks of clonic and tonic spasm spreading over the limbs, of a minute's duration, occurred during the last few weeks of life. Emaciation set in, bed-sores appeared, sphincter control was forgotten or lost, the patient passing everything beneath him. Difficulty in eating and swallowing increased, the temperature rose slightly, and on September 13, 1890, he died, having scarcely reached the age of 24.

At the autopsy the grey matter of the frontal convolutions was thought to be slightly atrophic or thinned, but the brain was of good size, weight, and shape; on horizontal section the middle zone of each lenticular nucleus was found to be softened and discoloured over an area of about 1 cm. in length and breadth. Slight sclerotic patches were discovered in the aorta and some of its main branches. The liver showed an advanced degree of cirrhosis.

Of the microscopical examination the following points will suffice for our present purpose. There was possibly some slight diminution in the myelinated fibres of the cortex in the frontal regions. While the pia mater was somewhat thickened, there was no small-cell infiltration, or only slight and scattered; the blood-vessels in the grey and white matter of the cerebrum were in many places irregularly thickened and hyaline or sclerotic in appearance; fine granules staining black with osmic acid were often noted in the vessel walls. The thickening seemed to be due mainly to the presence of fine granular masses of this description. While occasionally small round cells were found in the neighbourhood of vessels, they were few in number by comparison with the appearances in a brain of a general paralytic used as a control. The arteries of the middle cerebral distribution, lenticulo-striate, &c., were examined specially, and showed the same hyaline or sclerotic alterations; there were small collections of granular material, sometimes homogeneous-looking, sometimes with nuclei, lying round the elastic lamina, and occasionally bulging into the lumen of the vessel. The spinal cord was normal.

The only remark that need be made at this stage in reference to the microscopical findings is that the vascular alterations cannot be said to resemble a true endarteritis obliterans; in fact, Homén does not use the word in his description, and never refers to actual changes in the intima.

*Case 5 (Homén's No. 3).—*Wilhelm K. was born on August 8, 1870. He grew up a plump and healthy boy till the age of 12; but in the autumn of 1882 he began to complain of a general feeling of tiredness, and his memory and mental powers seemed to deteriorate. His gait, at the same time, became somewhat uncertain, and about a year later his articulation was noted to be defective. His arms became stiff to move, so that he had difficulty in making use of them, and simultaneously tremors developed in them, while the lower extremities began to become spastic or rigid. Very gradually contractures appeared, more especially at the knee and hip. After three or four years the patient was so helpless as to be bedridden; he scarcely ever spoke, and then only with difficulty and great indistinctness; his mouth was usually open and saliva dribbled from it.

On December 11, 1888, he came under the observation of Homén. It was noted that his speech was reduced to the enunciation of an occasional inarticulate and unintelligible sound, yet he sometimes managed to express some words with comparative clearness, especially if he was excited or disturbed. He lay in bed with his limbs in a state of contracture and drawn up, and yet by an effort of the will they could be very considerably extended, though not completely. Tremor was particularly well marked in the hands and arms, less obvious in the head and lower extremities. He passed his urine and stools into the bed. Emaciation was pronounced. The pupils reacted to light; cutaneous reflexes were present, but the tendon reflexes could not be tested

because of the contractures. Some small bed-sores appeared. The patient gradually sank and died on October 17, 1889, aged 19.

At the autopsy a horizontal section through the hemispheres showed that the optic thalamus, caudate nucleus, and internal capsule were perfectly normal, whereas symmetrically placed in each lenticular nucleus was an area of softening and degeneration that had resulted in the formation of a cavity. This cavity was about 3 cm. long and spread downwards and backwards to the lower extremity of the nucleus. The tissues round it were somewhat softened. Rather more than one-half of the nucleus, in breadth, was involved in the lesion. No other pathological change was visible to the naked eye. A few small sclerotic patches were found in the aorta, more particularly in its abdominal portion. The liver was in a condition of advanced cirrhosis.

Microscopically the blood-vessels of the brain were in some places irregularly thickened by the presence of granular or homogeneous masses between the membrana fenestrata and the intima; this granular change was apparently of a fatty nature in some instances, in other places it seemed to be more definitely cellular. Other blood-vessels seemed to be widened. Small round-cell vascular infiltration was almost completely absent.

Round the diseased area in each lenticular nucleus the tissues were degenerated and infiltrated to some extent with cells; but no microscopical alterations were discoverable in the other basal ganglia or in the internal capsule. The spinal cord was normal.

Case 6 (Homén's No. 1).—Anna K., the eldest member of the K. family, was born on July 26, 1862. She was a perfectly healthy child and girl, who never suffered from any special illness, and who had menstruated regularly at a normal age.

Towards the end of the year 1882, when she was 20 years old, identical symptoms to those from which her brothers had suffered appeared in her case—viz., headache, tiredness, loss of appetite, weakness, and impairment of memory. A few months later her walking became defective and her catamenia ceased. Then generalized stiffness of the trunk and limb musculature set in, and her speech became less distinct. Very gradually the arms and legs became contracted, the elbows, hips, and knees being the joints chiefly affected, and tremor developed in the arms and hands. As a result she became so helpless that she had to take to her bed. Dysphagia was a marked feature of the case. Her mouth was usually open and saliva escaped from it.

On August 29, 1888, she came into hospital. She lay in bed, helpless and apathetic, with a silly expression on her face; indifferent to her surroundings, she passed everything underneath her: she could not speak, as a rule giving vent to a few inarticulate noises from time to time, yet occasionally she appeared to wake up and then could articulate one or two words, though with difficulty. She died from inflammation of the lungs on October 19, 1888, at the age of 26.

On *post-mortem* examination the middle parts of both lenticular nuclei were found to be spongy and softened in consistence; and to be of a patchy greyish-yellow appearance. The liver was profoundly cirrhotic.

Microscopically the central portion of the lenticular nucleus, on each side, over an area of about 1 to 2 cm. long and 1 cm. broad, was discovered to be in a state of commencing disintegration, with disappearance of nerve-fibres and cells, and slight small-cell infiltration. A few small circumscribed "endarteritic" changes were noted in the Sylvian vessels.

Fig. 10 is reproduced from Homén's paper, and represents his third patient, taken about four months before the fatal termination. It conveys an excellent idea of his condition; the fixed smiling expression,



FIG. 10.—Wilhelm K. (Homén.) Note the fixed, smiling expression, open mouth, contractures, and some emaciation. (From *Archiv f. Psychiat.*, 1892.)

open mouth, emaciation, and contractures of arms, hands, feet and legs are well shown.

Such, then, are the three cases observed and described by Homén, which form a clinical picture of so definite a type that it is difficult to imagine how anyone familiar with the author's publication could fail to diagnose the condition if occasion arose. We can only conclude either that the paper has been lost sight of, or that the affection is characterized by considerable rarity, for no other instance of the disease, seemingly, has since been recorded—i.e., during the last twenty years. Reference will be made at the end of this chapter to Anton's case, published in 1908. While it presents certain resemblances to the cases under discussion, I am not convinced that its inclusion in the series is justified. The resemblance of Homén's group to the other three is very intimate. If the duration and the fever are excepted,

there is little else in which the two sets of cases differ. There is the same insidious onset, without apparent cause, in young people who have always enjoyed good health, the same steady progression of symptoms, until the patient is bedridden and helpless; the same dysarthria, involuntary movements, rigidity and contractures; the same emaciation and fatal issue. It is interesting to note that Homén was struck by the odd way in which the patient was able to articulate, at one time better than another, as also by the fact that, in spite of contractures, there was often still a fairly wide range of voluntary movement if an effort was made. From the negative standpoint, the absence of ocular and pupillary symptoms, of loss to sensory tests, of definite alteration in the reflexes, beyond the difficulty in eliciting the knee-jerks owing to the muscular condition, and of impairment of "le langage intérieur," may be specified. On insufficient grounds, in my opinion, Homén came to the conclusion that he was dealing with one of the manifestations of syphilis hereditaria tarda, although he could obtain no parental history of syphilis, nor did any of his cases present unequivocal syphilitic stigmata. From the pathological point of view, moreover, his descriptions do not suggest syphilitic endarteritis. As there are no illustrations of any of his prepared material, we must judge to the best of our ability from the textual evidence. This evidence will be examined in a subsequent chapter.

Towards the end of his paper Homén declares that the clinical phenomena find a complete explanation in the results of the *post-mortem* investigations, but if his correlation of the two is scrutinized it is found to be open to considerable criticism. The tremors and rigidity he attributes to "cortical irritation" ("Corticalreizung"), as also the contractures, though probably in the later stages of the affection the nutritional element also entered into the causation of these; the difficulty in speaking and in swallowing, the open mouth and sialorrhœa are, in his opinion, all dependent more on "general intellectual deterioration" ("allgemeine Intelligenzabnahme") than on any local factor, and similarly with the incontinence of urine and fæces.

It is evident that he assigns more significance to the slight diminution in the myelinated fibres of the frontal region ("unbedeutende Verringerung myelinhaltiger Fasern"), the slight changes in the cells of the cortex ("geringe Ganglienzellenatrophie"), and to the scattered and irregular alterations in the cerebral blood-vessels, than to any other pathological defect. In spite of the fact that all of his cases were found

to have bilateral lenticular softening, he does not refer to it specifically in such a way as to show that he attributes any of the clinical phenomena to its presence. There is no hint of any special importance to be attached to it, no reference to the association of dysarthria and involuntary movements with disease of the basal ganglia, no distinction drawn between pyramidal and extrapyramidal motor disturbance. The remarkable problem of the association of cirrhosis of the liver with degeneration of the lenticular nucleus, as opposed to other basal nuclei, is apparently not mentioned. No one who is interested in the disease will undervalue the splendid contribution of Homén, but the essential and fundamental features of the affection must be interpreted in the light of more modern knowledge of cerebral physiology.

Reference has already been made more than once to an article by Anton, which appeared in the *Münchener medizinische Wochenschrift* for 1908, under the title "Dementia choreo-asthenica mit juveniler knötiger Hyperplasie der Leber." In this communication Anton describes the case of a young girl, aged 14, whose development was very defective, as she corresponded in size to a child of 8, and who had always been weak and easily tired. In her early years at school she had been noted for "making faces," inattention, and unmannerly behaviour, especially at meals. Thereafter her gait gradually became stumbling, her control over her limbs ineffective; she let things fall out of her hands, and her handwriting deteriorated. When she came under observation it was remarked that she stuttered; involuntary choreiform movements occurred, interfering with voluntary acts; her gait was ataxic. The reflexes were increased. Glycosuria was present. Her mental condition varied very much; she seemed facile and simple, but tired readily and then became uncommunicative. Later, her mental and physical condition became definitely worse. Her speech became dysarthric, she kept her mouth open, and often had attacks of impulsive laughter; her limbs sometimes trembled, but amorphous and inco-ordinate movements were more frequent. Mentally she degenerated profoundly, at length becoming definitely demented. Towards the end convulsive attacks occurred, with conjugate deviation of the eyes to the right. She died from heart failure.

At the autopsy the first left frontal convolution, and part of the second, were found to be softened over an area extending almost from the frontal pole to a point about 2 cm. in front of the precentral convolution. The pons was atrophied. The right suprarenal was

atrophic in its lower third. The genitalia (internal and external) were infantile. The liver was typically cirrhotic, its nodules varying greatly in dimensions, and hypertrophied. On microscopical examination there was much thickening of cerebral blood-vessels, especially in the frontal regions, but also in the cerebellum. The softening in the left frontal lobe was a gumma. The putamen on both sides was softened, and the external capsule partially so. The anteromesial part of the optic thalamus was poor both in fibres and cells. Small-cell infiltration was noted, more particularly in the cerebellum.

This case is interesting from several points of view, and it presents certain analogies to the cases already mentioned, which need not again be specified. Pathologically, however, there seems to be no doubt of the syphilitic nature of the case; it must, therefore, be classified as congenital cerebral syphilis. The frank infantilism, the glycosuria, the complete dementia, find no counterpart in any of the other cases, or in my own. The case is of value, however, for this reason, that part both of the clinical and of the pathological features is in harmony with the findings in the other cases, especially Homén's, to which, indeed, Anton refers.

Such, then, is a brief sketch of all the hitherto recorded cases¹

¹ In the course of further search through the literature, while this paper was in the press, I came across a case under the observation of Frerichs, of Berlin, in the year 1854—i.e., fifty-seven years ago. It is recorded in his classical *Treatise on Diseases of the Liver*, and will be found in the second volume of Murchison's translation, published by the New Sydenham Society in 1860, p. 60. There is no doubt in my own mind that this case is one of the acute variety of progressive lenticular degeneration, and the fact that the essential clinical features of the disease can readily be recognized from a description of nearly sixty years ago affords striking proof of the specificity of the condition. The following extracts will suffice:—

"Carl Zeppner, a peasant's son, aged 10, was admitted on June 1, 1854. Up to a year before admission this boy had enjoyed good health, and in bodily and mental development had not been behind other children of his age. After bathing on one occasion, when he had been violently plunged by his companion with his head under the water, and kept there for some time, he complained of headaches and lassitude, became oblivious, began to stammer and to speak slowly and with difficulty, and gradually lost the power over his extremities. He often kept his bed for days on account of weakness; and when he wished to use his limbs, they were thrown into violent tremors. In other respects, his intelligence was not impaired, and his sensibility not diminished. Since Christmas he had completely lost all power of speech, and had been unable to swallow any solid food. . . .

"On admission, the boy appeared somewhat emaciated, but in other respects there was nothing else of an abnormal character to be observed in his external appearance. He was unable to stand or sit upright, or to hold anything in his hands; all movements were possible, but were performed very slowly and awkwardly; the sensibility was unaffected. His countenance exhibited an air of indifference, and failed to express either pain or pleasure; when the boy was told to distort his features, scarcely perceptible movements of the muscles of the face ensued. . . . The mouth opened slowly and incompletely. The tongue, which appeared somewhat flattened, but which was in other respects normal, was seized with a feeble tremor when the patient was ordered to move, or protrude it, or speak; the prick of a needle, however, could be felt in both halves of the organ. . . . The patient could swallow nothing but liquids, and even these with difficulty. . . . From time to time the difficulty of deglutition increased, and at the same time the movements of the extremities were imperfectly performed. . . ."

of the disease which I propose to call "Progressive Lenticular Degeneration." They constitute a little known chapter in nervous pathology, and present problems which it will be the purpose of this monograph to attempt to elucidate.

CHAPTER II.—CLINICAL CASES.

IN this chapter the clinical histories of four personally observed cases are given in detail. The pathology of three of them will be described in the next chapter.

The first case that came under notice (S. T., Case 1) was that of a patient under the care of Sir David Ferrier in the National Hospital, Queen Square, in 1905. At that time I was not aware of the cases which have been sketched in the previous chapter, but it was certain that S. T.'s case was one of a nervous disease which did not correspond to any familiar type. Sir David Ferrier considered that while it bore certain resemblances both to disseminated sclerosis and to paralysis agitans, it was quite distinct from either. A year later the patient whose case is No. 2 (D. P.) came into hospital under the care of Dr. Ormerod, and whenever I saw her I recognized that her condition was identical with that of S. T. (Case 1), who had been in the hospital a year previously. It was this case that supplied the clue to the mystery, for the patient died not long afterwards, and at the *post-mortem*, made by Dr. Stoddart, of Bethlem Hospital, and myself, an unsuspected cirrhosis of the liver was discovered. Gowers meanwhile had republished his two cases in the *Review of Neurology and Psychiatry* [4], and they at once threw the illuminating ray for which I had been waiting

An acute attack of what seems to have been dysentery supervened, and after a few days of fever, violent diarrhoea, delirium and convulsions, the patient succumbed.

"The body was emaciated, but there was no oedema. The muscular tissue was atrophied. . . . The cerebral membranes were much injected. . . . The substance of the brain was soft. . . . everywhere it contained much blood. . . . Nothing abnormal could be found in the substance of the brain. . . .

"The spleen was enlarged—6½ in. long, 4½ in. broad, and 1 in. thick. . . . The liver was small. . . . Its surface was covered with nodules, varying in size from a pea to a bean, and similar formations could be found in its interior, where they were separated from one another by broad bands of areolar tissue. The consistence of the organ was tenacious and leathery."

The resemblance is perfect. The youth of the patient, his previous normal development, the onset of dysarthria, dysphagia, weakness of the limbs, and tremors; the later emaciation, slowness of muscular movement without paralysis in the strict sense, the expressionless face, the increasing dysphagia and anarthria, the absence of any symptoms referable to the liver, and the intact sensibility, form an unmistakeable clinical picture. In spite of the fact that during life the symptoms are exclusively nervous, the sole significant pathological finding is extreme cirrhosis of the liver. In view of the acuteness of the lenticular disease the cerebral lesions are no doubt mainly associated with the severe illness of the last week of the patient's life. The same explanation holds good in this instance as in the acute cases recorded by Gowers.

over the darkness that enshrouded the others. Case 1 was followed up without delay, and a year later the autopsy revealed what was fully expected—viz., cirrhosis of the liver and lenticular degeneration. Case 3 was the brother of Case 2, and from beginning to end he was under my observation; in his case also similar pathological findings were obtained at the autopsy.

Case 4, which I owe to the kindness of Dr. Tooth, is that of a patient (M. To.) who was under his care in the National Hospital for a short time in October, 1911. The patient at the time of writing is still living. The clinical picture which her case presents is exactly that of the other three personal cases.

Two other cases, Nos. 5 and 6, will be found in this chapter. Case 5 is that of a patient referred to by Gowers as the eldest brother of his own two patients: "He was in the National Hospital six or seven years before, and died from some form of paralysis at the age of 15." A little trouble taken in tracing the movements of the M. family enabled me to find the mother of these patients, an old but vivacious lady, aged 70, and from her lips this history was obtained, which therefore makes the story of the M. family complete.

Case 6 is referred to in Ormerod's paper as follows:—

"A boy, aged 13, was under the care of Dr. Gee (at St. Bartholomew's Hospital) with ascites, anasarca, enlargement of the spleen, and purpuric spots on the legs. . . It was noticed before he left that he walked very badly. Subsequently he was admitted to Queen Square Hospital, under Dr. Thomas Buzzard, for nervous symptoms, mainly consisting of contractions of the limbs. He died, and the only definite lesion found *post-mortem* was cirrhosis of the liver." This case has never been published *in extenso*, and I am able to utilize it to render the record as complete as possible.

Case 6 presents certain features which distinguish it from the others, and in fact it is not clear, as in Anton's case also, that it is one of identically the same disease, but the resemblances are sufficiently close to warrant its insertion. In any case it sheds light on the etiology of the condition by analogy, if not directly, and for that reason it appears to me valuable.

Case 1.—S. T. was born on October 19, 1878. She was the youngest but one of the following family of nine:—

- (1) Female, born 1859, living and well.
- (2) Male, born 1861, living and well.

- (3) Male, born 1862, died in infancy.
- (4) Male, born 1868, died of diphtheria at the age of 15.
- (5) Female, born 1869, died in infancy.
- (6) Male, born 1875, living and well.
- (7) Male, born 1876, living and well.
- (8) Female, born 1878, died in 1908, aged 29 (Case 1).
- (9) Female, born 1881, died in infancy.

Family history.—The father died, aged 68, of appendicitis. He had always been a healthy man, but is said to have been "highly strung," and of a somewhat neurotic temperament. The mother died, aged 65, of cancer. There was no history of any form of venereal infection in the family.

Previous history.—The patient was always a perfectly healthy girl, the only recorded illness being diphtheria at the age of 5. Her catamenia began when she was 14, and continued regularly for a year or two; thereafter she suffered from a certain amount of dysmenorrhœa for some years, but at the age of 20 the periods became more regular again. She was a well-developed, active girl, and used to be an excellent swimmer. Her mental development was rather above the average; she was fond of literature, and at school was considered to be of an original turn of mind.

Present illness.—In 1899, when the patient was 21 years old, and during a sojourn on the Continent, she had an attack of jaundice, of about five weeks' duration, but further details as to this illness are not forthcoming. For some years thereafter she suffered at intervals from slight swelling of the legs, which used to be puffy round the ankles, and she "used to make dints in them with her fingers." There were no other symptoms, and she was never laid up or incapacitated in any way by it.

In May, 1904, when she was 25 years old, she went to live in Schwalbach, and while there it was noticed for the first time that her right hand shook a little as she was writing, and that her articulation was not as clear as it had always been. She began to slur her consonants and the ends of her words. She seemed quite well in her general health, and her friends were at a loss to account for the symptoms.

By September of the same year her condition had altered definitely for the worse. There was a change in her disposition: she became restless, and appeared "unable to settle to anything," and it was remarked how easily she was provoked to laughter, the most trifling incidents causing her to smile spasmodically. The tremor became much more pronounced; it was noticed on both sides, and in the arms as well as the hands and fingers. Her speech became more slurring, and a certain slight difficulty in swallowing developed.

At the end of the year she was seen in consultation by Sir David Ferrier, who was at once struck by the curious appearance of the patient, her almost silly smile, her more or less constant tremor, and a certain fixity of expression, which led him to wonder whether he might not be dealing with a case of incipient paralysis agitans. Examination convinced him that there were no signs of organic disease of the central nervous system, in the ordinary sense;

there was no nystagmus; the reflexes were normal; a double flexor response was present. Accordingly he sent the patient into the National Hospital, Queen Square, for further examination and observation, on February 24, 1905, in the twenty-sixth year of her age.

She remained in the hospital for almost two months, and during this time was repeatedly examined. At no time during her stay were any of the accepted signs of organic nervous disease present, so that more than once the suspicion that her condition was hysterical crossed the minds of those of us that examined her. Yet it soon became evident that the progressive nature of the disease excluded hysteria, and as disseminated sclerosis, another possible diagnosis, was not at all probable, the question of the exact nature of the disease was left open.

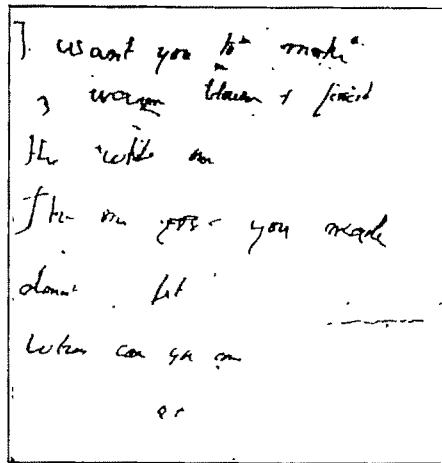


FIG. 11.—Handwriting of S. T. when in hospital.

The clinical picture which the patient presented was very striking. With a perpetual smile on her face, her mouth open, her limbs shaking, she moved slowly about the ward, often making very personal and apposite remarks about her fellow-patients; at other times she kept her bed, unable or refusing to speak when urged to do so. Her mental condition was curious; she showed an abnormal cheerfulness incompatible with the serious nature of some of the other symptoms: sometimes the expression on her face was fatuous, or silly, at other times she evinced considerable interest in things that would appeal only to an educated mind. She told me, for instance, that she had been learning Norwegian, and that when opportunity arose she intended to pursue her studies in that language. As for the dysarthria, so marked a feature of her case, there was no word which she could not pronounce more or less distinctly on different occasions, yet she was frequently unable to pronounce test words, and often her speech after a minute or two became simply unintelligible.

There was sometimes distinct difficulty in swallowing, but this symptom also was characterized by variability. Her handwriting was almost unreadable (fig. 11) owing to the constant tremor of her extremities—a quick, fine, rhythmical tremor which sometimes seemed to vary with the attention paid it, but at other times was unmistakably of organic type, increasing with muscular effort. It was always well seen in the finger-nose test. The legs were affected with a similar tremor, also more noticeable during muscular effort. Her gait was usually slow and uncertain; her muscles were weak in proportion to their development, but there was no voluntary movement which the patient was unable to perform. The musculature, on the other hand, showed a slight degree of stiffness, especially in the fingers, which were constantly extended distally and flexed proximally.

In spite of treatment the patient lost weight while in hospital, and left on April 19, almost in the same condition as when she entered it; if anything, a little worse.

In the summer of the same year (1905) her increasing weakness and the possibility of her requiring nursing care for a lengthy period caused her friends to procure her admission as a voluntary boarder to the Holloway Sanatorium, Virginia Water. Here she remained for about two and a half years.

During that time the progress of the disease was slowly but steadily downwards, yet for a long time her general nutrition was satisfactorily maintained. From the careful notes of Dr. Sheila Ross, under whose more immediate care the patient was during her stay in the sanatorium, one or two excerpts will suffice to indicate the steps by which the illness progressed.

"August 17, 1905.—The hands are falling into a condition of contracture. The fingers of the right hand are flexed at the metacarpophalangeal joints while the phalangeal joints are extended, the terminal phalanx is hyperextended, especially in the third finger. The tongue is protruded with some difficulty, but is not tremulous. Patient walks unsteadily and turns with some difficulty, there is well-marked tremor in the legs, more particularly when she is fatigued. It is not easy to understand patient's conversation. Her manner is childish, but this is accentuated by her habit of using as few words as possible in conversation, owing to her difficulty of articulation.

"August 31.—The tremors are more marked in the right limbs than in the left. Sometimes they are severe.

"October 25.—The patient now spends almost the whole day on a couch, as her gait is very uncertain. Swallowing becomes more difficult, and she is occasionally dirty, especially in the morning; for the first half-hour after waking she seems stupid, incapable of emptying her bowel or her bladder, and as a result is sometimes wet and dirty. All the deep reflexes are normal; there is a double flexor response. The pupils react well to light.

"January 3, 1906.—Patient's gait is feeble and stiff; her limbs are in contracture and rigid. Speech is very defective; she usually spells out words on a card instead of speaking, but occasionally, if suddenly asked a question, she responds in a few words readily. Saliva dribbles constantly from her mouth,

and swallowing is very difficult. The coarse tremor of the right hand has increased, and on the left side tremor and contractures of the fingers are more noticeable. Patient menstruated last month.

"April 21.—Mentally she is very self-absorbed, frequently calling the nurses to her, and annoyed unless their whole attention is given to her. She can walk a little, on her toes chiefly, if supported by two nurses. In spite of the severe dysarthria she occasionally brings out a few words fairly smartly. Her physical condition is good.

"October 27.—When making any muscular effort saliva dribbles from her mouth and she appears to be unable to swallow it. She has menstruated again."

In view of the conclusion I had by this time come to, that the case was one to be relegated to the category of Gowers's so-called "tetanoid chorea," in other words, that it was a case of lenticular disease associated with cirrhosis of the liver, I took an early opportunity of going down to Virginia Water to examine the patient, whom I had not seen for about two years, for myself. I am deeply indebted to Dr. W. D. Moore and Dr. G. W. Smith for their kindness in affording me every facility in this connexion.

I saw her on March 14, 1907, when she was about 28½ years old, and made the following notes at the time.

The patient looks remarkably plump and well; she is exceedingly sunburnt, and gives an impression of good health. She is able to get up daily, and walk a little, only a few paces, but she can neither dress nor feed herself. She takes an intelligent interest in what is going on, recognizes her friends and visitors, her nurses, the doctors, and often endeavours to speak, but never with any persistence. She knows quite well when she is physically comfortable or the reverse; her disposition is more than ever facile, almost childish; she never cries, but, on the other hand, laughs on the slightest provocation, in fact without any provocation. Her features are usually fixed in a broad smile, showing most of her teeth. Her mouth is always open, her lips retracted, her jaws apart. (Compare figs. 12 and 13.) Saliva escapes from her mouth. She looks, at a first glance, and until one begins to examine her carefully, a semi-imbecile, living in a restricted microcosmos of her own. It is soon apparent, however, that the impression first conveyed is erroneous.

She recognized me at once, although we had not met for two years, and proceeded to spell out my name correctly on her alphabet, her fingers and forearm in a violent tremor the while. Her attention and memory were unexpectedly good; she proceeded to remind me of incidents that had happened during her stay in the National Hospital, and even of one or two of her former fellow-patients. It is true that her means of conveying to me what was in her mind were not particularly effective, but the defect was solely one of execution. During the whole of my examination she never failed to appreciate

what I requested her to do, and obeyed to the best of her ability. She did not complain of anything, she did not suffer from headache or giddiness.

SPEECH.

There is, to all intents and purposes, a condition of complete anarthria in her case. She never speaks at all under ordinary circumstances, preferring to use her alphabet, at which she is an adept. When she spoke on my request, what she said was unintelligible. I could not catch a single word. As her mouth was fixedly open, her lips and tongue stiff and almost immobile, the sounds seemed to come directly from her throat; it was curious to see her "speaking" when her face remained completely motionless. I was told, however, that sometimes when the patient seemed quite at her ease, and was not consciously making an effort, the articulation improved a little and some words could be distinguished.

There is neither word-blindness nor word-deafness. Writing is impossible.



FIG. 12.—Photograph of S. T. before the onset of the symptoms of progressive lenticular degeneration.

CRANIAL NERVES.

Vision is good. There is no restriction of the visual fields. The optic discs are normal. The pupils are regular and equal, of medium size, and react well to light and on accommodation. All ocular movements are good in range and free in all directions. Convergence is quite good. The patient,

however, is unwilling or unable to sustain any of the movements for longer than a few seconds. It is noteworthy, too, that when left to herself her eyes "dance" slightly before her gaze comes to rest on a given object. On testing her, however, there is no nystagmus in any direction.

The corneal reflex is present on both sides. There is no impairment of sensation over the face. The muscles supplied by the motor fifth contract well; she can close her jaws, and bite voluntarily, but the movements are



FIG. 13.—Photograph of S. T., taken at Virginia Water. Characteristic appearance of face and upper limbs. Compare with fig. 12. [For this photograph I am indebted to Dr. G. W. Smith.]

certainly slow, and she appears incapable of sustaining the effort, for her jaws open again almost as soon as they are closed. She cannot move her inferior maxilla well from side to side.

The ordinary expression of the patient's face is well seen in fig. 13. There is a spastic smile which is rarely relaxed, and is often aggravated into a spasmodic laugh. The upper part of the face moves well on volition; the orbicular muscles of the eye contract; the patient can wrinkle her forehead, frown,

&c., satisfactorily; the lower part of the face, however, is almost immobile; she cannot whistle, cannot purse her lips up, cannot blow out her cheeks. She can bring her lips together slowly, but the movement is not sustained.

There is considerable difficulty in swallowing, the food escaping from the corners of the mouth, or remaining on the tongue. Sometimes choking results. The palate moves well and symmetrically on phonation. It also moves when the fauces are tickled.

The muscles supplied by the eleventh nerve are very hypertonic, but the patient is able to turn her head to the right or to the left slowly.

The tongue is thin and looks atrophic; it is narrower in its middle part, relatively, than at the anterior part; it is slowly protruded with considerable tremor, but there is no tremulousness or fibrillation of the surface, nor is it puckered or fissured.

MOTOR SYSTEM.

The general muscular nutrition is fair, but there is some slight general wasting of the muscles; the small muscles of the hands are thin, more particularly perhaps on the left side. The arms as a whole are thin.

(a) *Tone*.—The examiner is at once struck with the generalized hypertonicity of the muscles of the neck, trunk, and limbs. It is more pronounced in the upper than in the lower extremities. As a consequence, passive movements are accomplished with some difficulty. Thus, if the arm be passively flexed at the elbow the tone of the triceps is such as to give the observer a sense of considerable resistance, and a similar phenomenon occurs when the arm is passively extended. The same thing may be observed almost at any joint. The neck muscles are very rigid; even when the patient lies down the sternomastoids are not relaxed. On passive movement the lower extremities feel very stiff. Direct muscular excitability is increased.

(b) *Power*.—Voluntary movements are greatly hindered by the spasticity. Yet the patient can by a voluntary effort flex and extend at all joints, can abduct and adduct at hip and shoulder, can rise to a sitting position with difficulty, can move fingers and toes. The movements which are least good are those at joints where contracture is most marked—viz., at elbows and fingers more particularly. The leg movements are relatively better than the arms. The actual power of the voluntary movements is certainly below the normal. They can be easily resisted by the examiner. There is, however, no paralysis anywhere.

(c) *Contractures*.—There is definite contracture of both biceps muscles; the long flexors in both forearms, specially the right, are in contracture; the left hand has adopted the interosseal position of paralysis agitans; on the right, the forefinger and second finger are extended and the thumb opposed to them; the other fingers are flexed into the palm (fig. 14). The terminal phalanges of the left fingers are hyperextended. In the legs there is some contracture at hips and knees, and the feet incline to the position of equino-varus. By careful

passive movement, however, it is possible to overcome much, though not all, of the contracture. The segments of the limbs where it seems most established are the distal. It is a curious fact that, though the patient sits in a chair with the general attitude of a double hemiplegia with contractures, the attitude is not really fixed, for there is still considerable voluntary command over the muscles, and by an effort the limbs can all be straightened to a certain extent.

(d) *Tremor*.—Undoubtedly the most interesting feature of the case from the motor standpoint is the never-ceasing tremor. Whether the patient sits in the sun or lies in bed she exhibits tremors of the whole body that seem

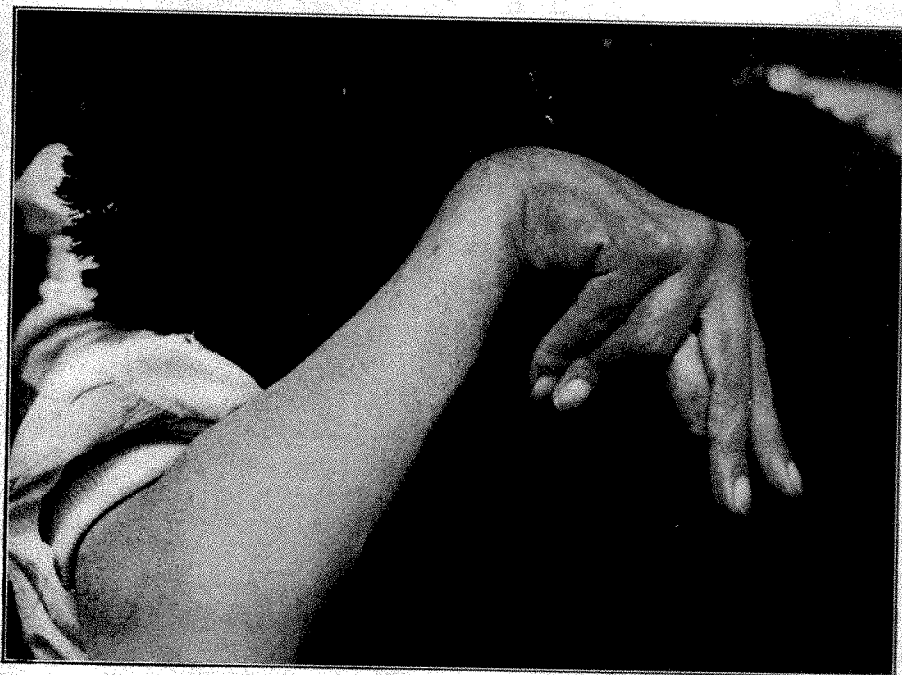


FIG. 14.—Right arm and hand of S. T., showing contractures, and resemblance of hand to that of paralysis agitans. (Exposure $\frac{1}{1000}$ sec., to obviate effects of constant tremor.) For this photograph I am indebted to Dr. G. W. Smith.

interminable. Even though she appears to be in a state of rest—i.e., well supported at all joints—the tremor never disappears. It is at once aggravated by any volitional effort, however slight, and it is made almost violent in such tests as the finger-nose test. It is particularly well seen when the patient endeavours to pick out letters on her alphabet.

In type it is usually quick and rather coarse—i.e., through a range of not less than 1 in. (2.5 cm.). Often the excursion increases considerably. The tremor consists of a true alternating rhythmical contraction of any given muscular group and its antagonists. In the arms the greatest movement is from

the elbows; the fingers and wrists are very stiff and move with the tremor from the upper arm. There is also, however, some interosseous tremor and slight tremor of the forefinger and thumb approaching to a rotatory type. The head moves with a slight to-and-fro tremor, and so does the trunk. In the legs the tremor is very well seen; even when they are at rest in bed it never ceases, and is at once aggravated by the slightest voluntary effort. The chief movement is one of flexion and extension at the hip, knee, and ankle, through a fine range, which is greater for the ankle than for the hip. There do not appear to be separate movements of the toes. I could not cause the tremor to cease entirely by supporting the whole of the limb, but undoubtedly it could thus be diminished in degree. The involuntary movements are never choreiform or athetoid.

(e) *Co-ordination*.—There is no real inco-ordination to be made out, as the patient is able to move her limbs in any given direction that is not prevented by the spasticity. When put on her feet she tends to fall in any direction indifferently, not from ataxia, but from the stiffness of her musculature interfering with her ability to keep her balance. When put in an upright position on the edge of her bed she falls backwards in a lump, the attitude of her limbs not altering in the slightest.

(f) *Gait*.—The patient requires very strong support, and can then walk a few paces, on her toes at first, more or less, but she gradually gets her heels down. The movements are highly stiff, tremulous, and uncertain.

SENSORY SYSTEM.

The patient does not complain of pain or paræsthesiæ, and on examination with the usual methods (touch, pain, temperature, deep sensibility) no definite alteration can be established.

REFLEXES.

All the deep reflexes are difficult to obtain, no doubt because of the rigidity of the muscles. They are present, however, though not brisk, and apparently equal on the two sides.

The abdominal reflexes are diminished on both sides, left more than right. An extensor response is obtained on the left side, and a flexor response on the right. There is no ankle-clonus. If the foot be pressed up on either side, the rhythmical alternating tremor of flexion and extension does not alter appreciably.

There is usually some incontinence of urine; it is not constant.

During the rest of the year her condition deteriorated step by step. Yet there was still an element of variability in the symptoms, often noted in regard to sphincter control. The anarthria became absolute, the contractures increased, and the patient began to lose weight. The tremor persisted without any change.

During the patient's stay at Virginia Water she was examined on several

occasions especially from the point of view of the functions of the liver. Notwithstanding that we expected to find a cirrhotic liver *post-mortem*, there were no symptoms of the ordinary kind associated with hepatic cirrhosis. In particular, there was neither ascites, nor œdema, nor distended veins, nor was there ever any icterus, even of slight degree. The liver was not palpable below the costal margin; its dulness in the nipple-line on the right side appeared, if anything, to be somewhat diminished. There were no symptoms referable to the stomach; no indigestion or sickness.

On January 29, 1908, the patient left the Holloway Sanatorium to live with her sister. She was examined before leaving, but no signs of physical disease, apart from the nervous system symptoms, could be discovered.

During the spring of that year her nutrition began to fail considerably, and she became very much thinner; with this increasing emaciation the contractions seemed to become worse, and all the symptoms were aggravated. She was utterly helpless, dependent on others for everything, anarthric and dysphagic, but at the same time she remained quite clear mentally, suffered from no delusions, was able to understand all that was said to her, and to express her wants in a way that could be understood by those around her.

In July, 1908, she was taken to be by the sea at an English watering-place. On Saturday, July 25, she was suddenly seized with an acute attack of hæmatemesis, vomiting 4 to 5 pints of blood. On Monday, July 27, she brought up a further 2 quarts of blood, and, sinking gradually, died on Tuesday evening, July 28, 1908, aged 29, after an illness of rather more than four years' duration.

RÉSUMÉ OF THE CLINICAL HISTORY OF CASE 1.

A young woman, aged 21, whose family history is negative, and who has never suffered from any particular illness, who has always been intelligent and physically active, suffers from an attack of jaundice of about five weeks' duration, the exact details of which are not forthcoming, and at intervals thereafter, for about two or three years, has occasional swelling of the ankles, without being in any way incapacitated thereby. Four years after the icterus, at the age of 25, she notices that her right hand shakes a little as she is writing, and her articulation becomes a little slurring. In the course of a few months her friends notice a considerable alteration in her general condition; she is restless, unable to settle to anything, easily provoked to laughter, constantly smiling and unnaturally cheerful. At the same time the tremor spreads to both arms and hands, her writing deteriorates, her articulation is definitely impaired, and she has some trouble in swallowing.

At the age of 26 she is examined by a neurologist, who can find no signs of organic disease of the nervous system, notes that there is no

nystagmus, and obtains a double flexor response. Nevertheless the condition is steadily progressive; the tremors are accentuated, the dysarthria and dysphagia increase, a generalized stiffness of the musculature reveals itself, and the fingers begin to assume certain attitudes of contracture. Her mental condition is one of facility; she is easily amused, and constantly laughing; her mouth is open and saliva occasionally escapes involuntarily. In spite of the vacant expression on her face her memory and perception are quite good; she has neither delusions nor hallucinations; she is very observant and often makes apposite remarks about those with whom she is associated. The symptoms are characterized by a curious variability; articulation and the power of swallowing seem sometimes to improve, and there is no true paralysis, in the sense that all voluntary movements can be carried out, though slowly.

During the next two years the disease slowly progresses. While for a long time bodily nutrition is well maintained, the other symptoms increase in severity. The features are fixed in a perpetual smile; the mouth is wide open and the sialorrhœa is more marked; the patient is anarthric and dysphagic; yet with voluntary effort the mouth can be slowly closed, the tongue slowly protruded, while the palate rises on the attempt to articulate; the pupils react briskly to light, ocular movements are free, and the optic discs are normal. The muscles become more and more rigid, the arms, and to a less extent the legs, fixed in attitudes of contracture, which can be to some extent, but not entirely, overcome by passive movement; as a result the patient has become peculiarly helpless; but again on volitional effort a considerable range of movement is still possible. The tremor is absolutely constant, often wide in range and severe in degree; it affects all muscular groups in the limbs, especially the distal groups, but includes also the lower jaw, head, neck and trunk. No sensory change can be detected; the deep reflexes are present without being exaggerated, there is no ankle-clonus; the abdominal reflexes are diminished, and the flexor response on the left side has changed to extensor, the other remaining as before. Defect of control over the sphincters, probably of central origin, appears.

Eventually emaciation sets in; the patient is reduced to a profound degree of helplessness, is in a state of contracture, speechless, incontinent; nevertheless her mental condition remains clear, she understands everything and endeavours to express her wants. An acute attack of hæmatemesis ushers in the end, and she dies at the age of 29, after

an illness of rather more than four years. With the exception of the initial symptoms nine years previously, there have never been either symptoms or signs referable to disease of the liver, but this is suspected during life and confirmed at the autopsy.

Case 2.—D. P. was born on March 6, 1887. She was the eldest of the following family of six :—

- (1) Female, died March, 1907, aged 19 (my Case 2).
- (2) Male, died September, 1910, aged 22 (my Case 3).
- (3) Female, aged 21, quite well.
- (4) Female, aged 18, quite well.
- (5) Male, aged 17, quite well.
- (6) Male, aged 13, quite well.

Family history.—The sole data of any possible importance are that the maternal grandfather became alcoholic in old age, and that a maternal uncle and aunt died of phthisis, the former at 35, and the latter at 28. There was no history of any nervous disease in the family; no history of syphilis on the part of either parents, or of gonorrhœa. The mother had had no miscarriages. At the time of writing both parents are alive and healthy.

Previous history.—The patient as a child was healthy and well nourished, so much so that she was called "Dumpy" by her parents. She was even-tempered and docile, and there were no mental peculiarities to lead to a suspicion that she was in any way different from other children. She never suffered from any serious illness at any time. She went to school, after private tuition, at the age of 14, and gave exceptional promise of doing well. Although she was a well-set-up girl, she never had menstruated.

Present history.—About the summer of 1904, when she was at school, and aged 17, it was noticed that she became rather untidy in her dress, where formerly she had been scrupulously neat. At the same time she began to lose flesh rather rapidly, and to look somewhat delicate. Her writing, which had always been good, deteriorated, and became "spidery." This was because of some difficulty in controlling the fine movements of her hands, and because of a quick, tremulous movement of the fingers. She took to writing in pencil instead of ink, and failed to obtain the same number of marks at school as formerly. This condition was ascribed to overwork, and the schoolmistress allowed her to do as she liked. The condition was progressive, however, and in June, 1905, she was removed from school and her parents took her to live with them in Italy.

It was then noticed that articulation was beginning to fail; there was a tendency for the lower jaw to drop, so much so that her parents would say, "Shut your mouth, D——," which command she would instantly obey, but in a short time the mouth was open again. A degree of general muscular weakness was observable, more particularly on the right side. It appeared to be "heavy"; nevertheless the patient could walk as much as four miles without feeling tired. Yet there was an element of awkwardness in her gait

which had not previously been present. At the same time her hands became more tremulous, especially if she felt that she was being watched. Her conversation became simpler, less intellectual, more childish; "her younger sister had to be a mother to her." In October, 1905, she developed some delusions. She chanced to pick a grape in a vineyard and thought that she was therefore wanted by the police. She also imagined that her father was a prisoner of the Pope. This delusional state, which was accompanied by some motor excitement, only lasted for a few days.

All the symptoms, the tremor, weakness, dysarthria, slowly increased in intensity. At the beginning of 1906 she occasionally suffered from spasmodic bursts of tears. Once when asked to make a choice from some articles for a present she could only smile in a spasmodic, silly manner.



FIG. 15.—D. P. before the onset of the symptoms of progressive lenticular degeneration.

The patient not improving, she was brought to England in the beginning of May, 1906, and seen by Dr. W. H. B. Stoddart, of Bethlem Royal Hospital, who after careful examination considered the case a nervous and not a mental one, and sent her to the National Hospital. When Dr. Stoddart (to whom I am greatly indebted for valuable help in connexion with this case) saw her he noted the following points:—

She was a tall, well-built girl of dark complexion, with a profusion of dark hair reaching to her waist. There was some pigmentation or discoloration in various parts of the body, especially round the ankles. She was not anæmic, but she had obviously lost much flesh. The tongue was dry and coated with a brown fur, and the breath somewhat offensive, but the teeth were normal.

Her general aspect was striking. The mouth was almost constantly wide open and the face wore a perpetual smile. The hands and arms were affected with a tremor that varied greatly in intensity from time to time, sometimes coarse, sometimes fine and scarcely noticeable. Owing to weakness and stiffness of her muscles she tended to fall to the right when standing or walking, or even when attempting to sit upright in a chair. She was childish in her behaviour; she laughed many times during the course of examination, and did not appear to realize the gravity of her condition. Her memory was unimpaired, and perception was perfectly good.



FIG. 16.—D. P. (National Hospital, May 1906). Note how patient is leaning over to the right side.

On May 11, 1906, the patient was admitted to the National Hospital, Queen Square, under the care of Dr. Ormerod, where she remained for almost a month.

She was carefully examined on many different occasions. She presented a striking clinical picture, some idea of which may be obtained from fig. 16. With mouth open, wearing a perpetual smile, she walked about the ward, moving slowly and tending to fall to one or other side, usually the right; she made childish remarks about trifling things in language almost unintelligible because of dysarthria, slurring the consonants and curtailing the last syllables, yet it was odd how this speech-defect could occasionally be overcome by an effort of the will. Her general appearance suggested a degree of mental

defect which was not nearly so pronounced as a superficial glance might convey. As I sat by her bedside one day I said jokingly, "Why, you're just a little girl," to which she replied quickly and with little or no articulatory defect, "I'm not a little girl!" as though to impress me with the fact that her looks belied her. Her attention was poor; ophthalmoscopic examination was difficult because of her unwillingness or inability to keep her eyes still. Her spasmodic laughter was remarkable; on slight provocation the smile on her face would broaden visibly and a curious laugh, with no "tone" in it, would escape in bursts.

The expression on her face was often rather vacant, especially if the otherwise fixed smile relaxed. There were no defects in the domain of the cranial nerves. The pupils reacted briskly to light. The optic discs were normal, and there was no defect of ocular movement, in particular no nystagmus. Facial movements could be carried out voluntarily, but somewhat stiffly; she was unable to whistle, and when left to herself kept her mouth constantly open. The palate moved normally, and there was little actual difficulty in swallowing. The tongue movements were not well executed; it was protruded slowly, but came out straight.

All voluntary movements were good in strength and range. There was an increased degree of tonicity in the muscles, but no contractures at this stage. When the upper extremities were at rest little or no tremor was noticeable, but when the patient made any voluntary movement it became very marked—a coarse tremor of hands and fingers, about four or six to the second, through a range of 1 or 2 in. (2.5 to 5 cm.). It was well seen in the finger-nose test. The same kind of tremor was present in the legs. Very occasionally, as she sat up in bed, a similar tremor, but finer in range, was observed to affect the trunk. There was no muscular wasting.

In spite of the patient's volitional control over her musculature, there appeared to be a rather disproportionate motor helplessness. When left to herself she would fall or roll about; owing to a generalized stiffness she could not, or would not, use her muscles to help herself, or keep herself from falling. This is seen in fig. 16, if the vertical lines of the curtain at the back are compared with the oblique position of the long axis of the patient's body. Her gait was slow, uncertain, stiff; her feet were kept apart, yet she had difficulty in maintaining equilibrium.

Sensation was perfectly normal. All the reflexes, cutaneous and deep, were normal. A double flexor response was constantly obtained.

As the patient's condition did not improve, and because of difficulty in getting her to take her food, she was transferred to Bethlem Hospital, under the care of Dr. Stoddart, on June 6, of the same year, 1906, being then 19 years old. From that date, until her death the following March, I had many opportunities of observing the progress of the disease, of which the following notes will convey some idea.

For some time she had to be tube-fed, because she was apparently under the impression that her food was poisoned, but this idea passed off, and she

did her best to take food voluntarily. She had, however, the greatest difficulty in swallowing it, and a few days before her death the dysphagia was so complete that tube-feeding had again to be resorted to. It is worth remarking that even when the dysphagia was greatest some efforts at swallowing were executed more easily than others, and that the reflex was present throughout.

Up to the end of 1906 the spasmodic smile was fairly well marked, but during the last two months of life it gradually diminished, and the facies became characterized by a complete absence of expression. The lower jaw dropped still more; even during sleep the mouth was open.

The tremor of the extremities became increasingly severe: its excursion was sometimes as much as 3 in. (about 7 cm.). Towards the end the tremor of individual fingers was more prominent than ever; it was usually antero-posterior, but sometimes lateral, the rate being about four to six a second. The tremor of the legs and trunk persisted. Weakness of the limbs increased almost daily; as late as the beginning of January, 1907, the patient was still able to stand, though only with assistance, but thereafter her helplessness became so pronounced that she was kept in bed. After this, contractures of the limbs set in with rapidity; at the elbows, hips, and knees the limbs were drawn up. The spine became very rigid. For some months before her death she was unable to protrude her tongue. The weakness and tremor were throughout more marked on the right side. In spite of every effort to maintain her general nutrition the patient gradually became emaciated, but there was no local muscular atrophy, nor was there more general wasting of the musculature than could at first be accounted for by the continued rest in bed, but towards the end the emaciation became extreme. Sensation remained normal throughout.

The knee-jerks were moderately exaggerated; there was no ankle-clonus at any time. The abdominal reflexes were never abolished; they were obtained on February 27, four days before the patient's death. The plantar reflexes remained of the flexor type on both sides, although during the last three days of life some variability was noted. During the early months of the year some weakness of the anal and vesical sphincters set in, not, however, of local significance, in all probability; the patient usually indicated when she experienced a call to stool, and was, therefore, generally kept clean; but if, at the moment, there happened to be no nurse in the room, the dejecta were passed into the bed.

From the time when the patient went to Bethlem Hospital dribbling of the saliva was a prominent symptom. At first handkerchiefs were used as bibs, but eventually it became necessary to employ a large towel, so profuse was the sialorrhoea. It was a remarkable fact that during the last week of the patient's illness this flow of saliva entirely ceased.

On the evening of February 24 the temperature rose to 101.2° F., and sibilant rales could be heard in various parts of the chest. Two days later there was a patch of dulness at the apex of the lower lobe of the right lung. The temperature varied from 101° to 103° F. During the last two days the respirations

became somewhat hurried, and were accompanied by dilatations of the aë nasi. The patient gradually sank, and died on the evening of March 3, 1907, being then 20 years old all but three days.

RÉSUMÉ OF THE CLINICAL HISTORY OF CASE 2.

A girl, aged 17, in whose family history no factor of any pathogenic significance can be discovered, and with a clean bill of previous health, with the sole exception that she has never menstruated, is noticed to develop a fine tremulous movement of the fingers, so that her handwriting deteriorates, to lose flesh, and to fail somewhat in her school work, so that she does not obtain the same marks as formerly.

Some six or nine months later, her age being 18, it is found that her articulation is becoming defective, and that she tends to keep her mouth open. A general muscular weakness appears, and the tremor of the hands increases. Her conversation becomes simpler and rather childish, and she suffers from one or two delusions, which, however, do not persist.

Rather more than a year from the onset of the disease, the tremor, weakness, and dysarthria have become more pronounced. She has occasional attacks of spasmodic weeping, but as a rule her face wears a stiff, spastic smile, her mouth is always open, her limbs show a more or less constant rhythmical tremor, which increases with muscular effort, and she has great difficulty in maintaining her equilibrium, owing to a generalized weakness and stiffness of the musculature. She laughs at trifling incidents, and often, indeed, without apparent cause, but on careful examination and observation it is found that she is not in reality suffering from that degree of mental impairment which her appearance suggests. She presents no ordinary sign of organic disease of the central nervous system; the pupillary, cutaneous, deep and organic reflexes are all normal.

In about two years or less from the beginning of the disease dysphagia becomes evident, she seems to be very helpless, falling about, and unable to maintain her balance, her muscles are both weak and hypertonic, but there is no true paralysis, as all voluntary movements can be performed, though slowly. The tremors and dysarthria become extreme. In spite of her perpetual smile and silly appearance, her perception is good and her memory unimpaired.

During the next few months, and in the latter part of her twentieth year, the disease runs a downhill course. Saliva escapes from her open

mouth. The hypertonicity of the musculature increases, her face is fixed and expressionless, her weakness and helplessness are profound. Contractures appear at elbow, knee, and hip, the tremor of the fingers, arms, trunk, and legs becomes coarser in type and is often violent, the dysphagia and dysarthria are such that maintenance of the patient's nutrition is a serious problem, while her speech is unintelligible, and in fact she scarcely utters a single word. Examination shows that there is no involvement of the pyramidal system, for the abdominal reflexes are always obtainable, and a double flexor response is constantly noted. Sensation is intact, the ocular movements are free, and there is no nystagmus.

At length, emaciated and in a state of contracture, she dies from bronchopneumonia, aged 20 years all but three days, three years from the commencement of the illness. Notwithstanding the fact that the patient has been exhaustively examined on many occasions, there are never any symptoms referable to the liver, nor has she presented any signs that might be associated with disease of that organ.

Case 3.—E. P., the eldest brother of the patient D. P., whose case is No. 2 in my series, and the second member of the family in order of birth, was born on May 14, 1888.

Previous history.—With the exception of whooping-cough at the age of 9, the patient passed a normal childhood and boyhood. He was active and intelligent, and never had anything the matter with him. He went to school at the age of 12½ years, and had an excellent scholastic record. Here he remained doing exceedingly well till Easter, 1906, when certain symptoms unexpectedly appeared, to the surprise and distress of his relatives.

Present history.—During the spring months of that year, when the patient was almost 18 years old, he had been working very hard for an examination and broke down under the strain. He found he could not concentrate his attention on his work. He was keen on athletics and had been playing football all winter, but games had to be given up. An attack of motor excitement accompanied by hallucinations of hearing suddenly ensued, and he became unmanageable. On two medical certificates he was admitted to Bethlem Royal Hospital, on April 11, 1906.

These certificates contained the following statements: "The patient is very excited and emotional, says he is being influenced, willed, or hypnotized to do certain things, is quite sure that God is working a miracle on his behalf. Says he has heard God and the devil talking to him simultaneously, and does not know which voice to obey. Is frightened because, although he has been baptized, he is not now certain whether that has secured his salvation."

On examination at the hospital he was seen to be a tall, well-developed

young fellow with a dark complexion. He presented no symptoms of organic disease of the central nervous system. His speech was normal; there was neither rigidity nor tremor; the pupils reacted briskly; all cutaneous and deep reflexes were normal. The urine contained no abnormal constituents. On the day after admission he already appeared to be more rational and his temperament was noted as being bright and cheerful. He admitted that about ten days previously he had heard the voice of God speaking to him, but now thought it might have been a dream. Voices in his ears which he then heard he said might possibly have been those of other people in the building.

During the summer his condition gradually improved. At intervals he was subject to hallucinations, and at these times he became excitable and restless, laughing and crying alternately, and suffering much from insomnia. By the end of July, 1906, with the exception of these attacks, which lasted about a week at a time, he was more himself again, and from that time he improved steadily. He was so well that on February 5, 1907, he was sent to the Bethlem Convalescent Home at Witley, not having shown any symptoms for months previously. He was discharged recovered on April 3, 1907, and went out to Italy to his parents.

Although submitted to several careful neurological examinations by Dr. Stoddart, he never showed any sign of organic disease of the nervous system, and the diagnosis of exhaustion or toxic psychosis seemed entirely justified. A good prognosis was given.

During the summer of 1907 he was very well. He took long walks and climbs, being away for twelve hours at a time, and never gave cause for any anxiety on the part of his parents. He was quiet and reserved, it is true, but he always had been of a rather retiring disposition.

Towards the latter part of the year, however, when he was 19, a different group of symptoms made their appearance and progressed with rather alarming rapidity. He began to have difficulty in speaking and swallowing, and his mother noticed how constantly a thin stream of saliva used to escape from the corner of his mouth. Further, his hands became tremulous, and his handwriting became very bad. He did not complain of anything, had neither pains, headache, nor giddiness, yet in three months' time his whole condition had altered appreciably for the worse.

During 1908 the disease advanced steadily. The tremor became generalized, the dysarthria more pronounced, so that he rarely spoke at all, the difficulty in swallowing did not diminish, and he had a constant tendency to let his mouth open, sometimes widely, without apparently being aware of the fact. His limbs, more particularly the legs, became stiff and weak, but there was no paralysis in the ordinary sense of the word, as he could move them well enough, and could walk about without any assistance. He was sent to be under the care of Dr. Reymond, at Chexbres, near Lausanne, and in a letter from his father, dated November 13, 1908, from which the following passages are taken, I received some information as to the patient's condition:—

" His main difficulty now is that he swallows badly and that his

articulation is very imperfect indeed. He is still troubled with an abnormal flow of saliva. Still, compared with his previous condition, I think there is improvement in each of these directions. When I saw him I certainly understood him better than some months previously, but articulation is most defective still. . . . As to his ability or inability to walk and stiffness of legs, of which you ask, I think there is some improvement. During the two days that I was with him we walked, and even climbed, a good deal, and it was I, not he, who always tired first. Dr. Raymond thinks that there is nothing wrong whatever with the boy's mental condition. Certainly in long and searching conversation, and in his various letters home, we never see the slightest sign at all of mental trouble. I do not think that I can say that the mind is equal to vigorous work. He reads a great deal, but does not ask for deep books. His

read it
Yesterday Uncle Edgar sent me the
Jan. number of the Shirley Mes-
senger.
I had such a nice letter from
Father which arrived on the 25th
of Dec.^r
Also a budget from the children.
at home.

FIG. 17.—Normal handwriting of E. P.

memory seems exceptionally strong. He writes very badly, and, if possible, gets someone to write for him. But he sent us last week an eight-page dictated letter, sensible, bright, and full of interest, exactly reproducing his thought as he gave it. This may have been dictated at more than one sitting, but it certainly means that the boy is quite able to express himself upon all ordinary lines, and, further, that he managed, whether with or without difficulty, to make his amanuensis clearly understand, at his dictation, eight pages of matter. Of his own handwriting I send you a specimen herewith. [Compare figs. 17 and 18.] . . . He looks to me a little stouter. . . ."

During 1909 the illness progressed slowly but steadily in a downward direction, and at the beginning of 1910 it became clear that there could be only one end to it, and that perhaps not very far off. I cannot do better than

quote some sentences from a letter from the patient's father, dated May 27, 1910:—

" . . . I am sorry not to be able to give you a good report of E——'s progress. As far as I am able to judge, the mind is perfectly clear, and I think on the whole the lad is happy. But there is a very distinct and marked failure in physical strength. . . . The symptoms are very greatly aggravated since I last wrote to you. He seems to have lost almost entirely control of his motor nerves. The effect of this is that he cannot grasp, that he swallows with so great difficulty that it is a serious matter to get him fed, and his power of articulation is so very slight that one can hardly understand a single word he

The image shows a piece of paper with handwritten text in cursive. The handwriting is extremely shaky and illegible in many places. A large, dark, diagonal ink stroke is drawn across the middle of the page, from the upper left towards the lower right. The text is written on lined paper. Some legible fragments include "Strength", "I am sorry", "progress", "mind is perfectly clear", "physical strength", "symptoms are very greatly aggravated", "lost almost entirely control of his motor nerves", "cannot grasp", "swallows with so great difficulty", "power of articulation is so very slight".

FIG. 18.—Handwriting of E. P. after the onset of progressive lenticular degeneration.

utters. Dr. Raymond has given him a kind of tablet with the alphabet in letters each about $1\frac{1}{2}$ in. square, at which he tries to point, to spell what he wants to say; but in any attempt to indicate a letter with his finger, the trembling, I could almost say the vibration, of his hand is so violent that it has to be held and steadied before it can reach a desired letter. He has lost control in some measure of the physical functions of the body in a way which makes the care of him difficult for others. He is wonderfully patient and of a happy disposition, though one can see that he suffers very much, naturally, at not being able to express himself. . . . This fact of itself, you will note, proves a considerable measure of balance of mind. . . . E—— cannot now get his hand

anything like steady enough to write a stroke; the poor fingers, when he tries to hold pen or pencil, shaking, or rather swinging, with a swing of two or three inches, or even more. His limbs are somewhat emaciated. He is not now strong enough to walk many paces. . . ."

As the patient had not been seen by any neurologist since the onset of the symptoms of progressive lenticular degeneration in the autumn of 1907, it appeared to me desirable to investigate his condition for myself. Accordingly, an early opportunity was taken of paying a visit to the sanatorium where he was living, and the greater part of [Saturday, June 4, 1910, was spent in examining him. The following description is based on the notes made at the time.



FIG. 19.—E. P. (June 4, 1910). Note mouth, contractures, tremor of the hands. (Exposure, $\frac{1}{100}$ sec.)

GENERAL AND CEREBRAL.

As I walked round the corner of the building and came upon the patient sitting in a lounge chair in the sun, the impression I received was one not easily to be forgotten (fig. 19). He was leaning back with a broad smile on his face, his mouth wide open and the saliva dribbling from it on to his chest, his arms and hands were in a state of contracture and drawn up, moving to and fro ceaselessly with a quick rhythmical tremor; his toes tapping the ground with a similar rhythm, his whole attitude one of vacant complacency.

If, however, this first impression was one of the utter helplessness of the patient, it was not long ere one perceived that it was to a certain extent erroneous. It is true he had apparently no idea who I was, although we had met several times previously, and he did not appear to show any signs of interest or recognition when I spoke to him of his mother. On the other hand, he evidently knew familiarly the various inmates and members of the staff of the place, and he could pick out with accuracy the various photographs of friends scattered about his bedroom.

His mental state was one of great facility; he was as docile as a child. He did whatever he was told to do, often with a brief, involuntary, explosive laugh. Aware of this mental condition, some of his fellow-patients would say, "Open your mouth, Mr. P.," and this he would at once do, to the accompaniment of bursts of laughter. He laughed constantly while he was being examined, yet when he noticed that one of the legs of my camera was unsteady he at once put out his left hand to hold it, though the movement was slow.

He read the English journals every day, and used his alphabet quite intelligently. He knew where everything was in his bedroom, or round about him, that was required for his use, although his gestures to indicate what he wanted seemed to me to be poor. Others, however, more familiar with him, could understand perfectly. He was hugely pleased with any little attention paid him; if his mouth were wiped he passed at once from his smile to his laugh. When his reflexes were being tested he burst into a loud "rire spasmodique," and I got a most distinct impression that he remembered that sort of thing having been done before. He was evidently acquainted with the use of all sorts of articles with which I tried him; he was, however, unable to do anything for himself, his movements being so very slow and laboured.

It was difficult to be sure whether he was correctly oriented in time; he appeared to be well enough aware of what was going on in his own little world. It was curious how quickly he noticed things; when I helped to dress him after examination he corrected me several times in my manner of doing it. He seemed quite happy and contented, and did not appear to have complete insight into his own condition. Nor could I interpret any of his actions or gestures as indicating that he suffered mental pain at being unable to express himself. He appeared to have little initiative or spontaneity, although, I suspect, this may possibly have been due to some consciousness of his helpless condition.

As for his general physical condition, he was tremendously sunken, but very thin. There was not an ounce of fat on his body. The outlines of the muscles and tendons were everywhere clean cut. The vertebral spines were very prominent. The face was comparatively well nourished. The genitalia were well developed, and there was a good deal of pubic hair. The feet were somewhat oedematous, and the ankles a little puffy, but this oedema could not be dimpled with the finger. There was no abnormality, however, of heart or circulation.

Perhaps the most striking feature of his case was his complete helplessness,

and the indifference bred of a knowledge of this. He sat in the sun in the chair, rolling over to one or other side if he lost his balance, the extraordinary hypertonicity of his musculature making the effort to recover himself almost useless. I found him, on one occasion, leaning right over the arm of his chair, the fixed smile on his face, apparently content to hang thus until he was found and put back in position. His indifference was sometimes remarkable. On several occasions he kept his mouth wide open long after I had asked him to open it; similarly he once kept his tongue protruded for several minutes. Occasionally the smile relaxed and the vacant expression became less obvious, but he never seemed to express any other emotion, and made no visible facial response when I gave him messages from his parents, or when I finally said good-bye.

SPEECH.

During the whole time we spent together he said only three or four words, of which two were, "I will." These words seemed to come from his throat, after the fashion of a ventriloquist, for there was no appreciable movement of lips or tongue. His anarthria was complete. So too, practically speaking, was his speechlessness; he made no effort in response to my urging him at least to attempt it. Nor did he appear distressed at this.

On the other hand, he used his alphabet with perfect correctness, spelling out such words as "doctor" without any difficulty. He appeared to be able to read quite well, and to understand what he read. Various drawings of familiar objects he recognized easily. He never once failed in the whole of the examination to perform correctly what he was asked to do—with the exception of the speechlessness—although, of course, the actions were very slow. There was no apraxia to be detected, and no agnosia. It struck me as affording a remarkable contrast, this *apparent* imbecility, compared with his quickness in appreciating everything the examiner did, or said, or asked. When I proposed going inside the house he at once tried to get on to his feet; when I asked for a towel he indicated where to find one; when I requested him to do this or that for the purposes of photography he co-operated with the greatest intelligence. Thus to apply the term dementia to his mental condition would be inaccurate. Writing was impossible.

CRANIAL NERVES.

Vision was good. The visual fields were normal. The optic discs (emmetropic retina) presented no visible abnormality. Ocular movements were good in all directions, and there was no trace of nystagmus. Sometimes the ocular movements seemed better sustained than at other times, but this was solely a question of attention. When the patient moved his eyes about of his own accord and not to command, it was noted that there was occasionally some unsteadiness in fixing an object; this, however, was only momentary.

The pupils were regular, equal, and of medium size; they reacted briskly to light, and contracted well on accommodation.

The corneal reflex was brisk on both sides. There was no sensory impairment over the face. The motor fifth muscles contracted well. The masseters contracted so that the patient could close his mouth, but the movement was slow and not well sustained, as the patient was in the habit of keeping his mouth widely open. Opening of the mouth against resistance was unexpectedly powerful. The whole of this musculature was hypertonic, and the patient had difficulty in moving his jaw from side to side.

Except when the patient's face was contracted into a broad smile, he had an utterly stolid, mask-like facies, the facial lines round his mouth being obliterated, and the latter simply an aperture in the mask; the lips themselves, however, did not hang much (compare figs. 20 and 21). Frequently he wrinkled his forehead and made other movements of the upper face, but his



FIG. 20.—E. P. in his school days.

mouth never moved except when he went off into the smile or laugh, which, it is true, occurred almost every minute. On attempting to whistle only a feeble contraction of the orbicular muscles was detected, and he was unable to make any sucking movements. When urged to show the teeth—i.e., to retract the corners of his mouth—he indulged invariably in a spasmodic laugh, so that it was difficult to gauge the amount of voluntary movement. He could wrinkle the forehead, frown, close eyes tightly, &c., quite well to order. When the muscles contracted into a smile it was always a stiff, tonic contraction, which did not relax quickly, and often remained fixed, one might almost say pinned, on the patient's face. The fact that the lips did not hang down showed the tonicity of the musculature.

Hearing was normal on both sides.

The palate moved well and symmetrically in the effort to phonate. The patient usually succeeded in saying "ah" very fairly. The palatal reflex was present on both sides. Swallowing was very bad indeed. He could not make the movement of swallowing on request. Water he swallowed in gulps, noisily, a great deal of it swimming about in his mouth and running out at the corners. He was unable to approximate his lips sufficiently to grasp the edge of the vessel adequately.



FIG. 21.—E. P. (June 4, 1910). Note vacant expression, open mouth, sialorrhœa, contractures. (Exposure $\frac{1}{250}$ sec., to counteract effect of constant tremor.)

No paralysis of the muscles supplied by the spinal accessory nerve was noted.

The tongue was thin and narrower from side to side in its middle section than nearer the tip. When he protruded it to command, there was much to-and-fro tremor as it moved slowly forward, but he managed to get it right out, and once it was well out the tremor ceased. Lateral movements were also performed, though very slowly. There was no fibrillary tremor, nor was it cracked or fissured.

MOTOR SYSTEM.

General muscular development was fair, but at the same time the musculature had obviously been shrinking and was in a state of poor nutrition. There was no local muscular atrophy to be observed anywhere, and no fibrillation.

Tone.—All the skeletal muscles, almost without exception, felt very firm to the touch, and this hypertonicity was probably one of the reasons for the slowness of the patient's voluntary movements. There was always a certain difficulty in impressing any passive movement on a limb, but it could be effected. If the arm was passively extended and flexed quickly at the elbow, insufficient relaxation impeded the movement; if it was done more slowly there was no difficulty. When any limb was placed in such a position as to relax the muscles as completely as possible it was found that they still felt firm. When the patient was voluntarily contracting, say, the left biceps, in the effort to flex at the elbow against resistance, the left triceps did not relax entirely, though it became for the moment less tonic.

The abdominal and the leg muscles were similarly rigid, palpation of the abdominal viscera for this reason not being easy.

The results of this generalized rigidity were rather curious. The patient seemed to be "soudé"—i.e., welded or soldered, after the picturesque French expression. He fell about *en bloc*; his back moved *en bloc*; sitting on the edge of his bed he would slowly lose his balance and fall over in a solid mass on to his side, often to his huge delight, at least in the presence of a visitor. The neck muscles were always in a highly tonic state; even when he lay with his head back on the pillow the sternomastoids did not relax. It was clear that the condition of the musculature had a great deal to do with the difficulty experienced by the patient in maintaining his equilibrium.

Speaking generally, the spasticity was more evident in the trunk and proximal sections of the limbs, whereas the tremor was most noticeable in the distal portions of the limbs, and affected the proximal joints and the trunk to a less extent.

It cannot be said that there was any specialized local myotonia. For although relaxation was slow, it was no slower than voluntary contraction; they were alike in this respect, nor was there any distinction between flexor and extensor groups, or between any muscular group and its antagonists, in the matter.

Contractures.—The hands and arms were, when left to themselves, held invariably in the position to be described (fig. 21). On the right side the forefinger was flexed at the metacarpophalangeal joint, but extended distally, and similarly with the thumb. These two fingers were in opposition, whereas the other three fingers were flexed at all the joints. The wrist was flexed to a right angle, the forearm semipronated and flexed on the upper arm, which was adducted at the shoulder. The whole position of the arm was suggestive of the attitude adopted by a hemiplegic limb with contracture, while there was a distinct resemblance to the attitude of paralysis agitans in the hand (fig. 22).

The left hand was curled up, with the thumb held inside the flexed first and second fingers; the wrist was not so much flexed as on the right side; the arm was flexed at the elbow and adducted at the shoulder.

The lower extremities were flexed at the knees, not to a great extent; the feet were somewhat inverted and the heels drawn a little up. The toes were slightly flexed.

As has been said, if the patient was left to himself, such were the apparent contractures of the limbs, and they never varied. But the interesting thing was that these were really "contracture-attitudes" which could be overcome, both actively and passively, to a very large extent, so that the degree of true permanent contracture could be estimated. It was found that the right arm



FIG. 22.—E. P. (June 4, 1910). Contracture-attitude of right hand. (Exposure $\frac{1}{150}$ sec., to obviate the effect of never-ceasing tremor.)

could not be completely extended at the elbow, nor could the legs be completely straightened at the knees. Apart from this the limbs could be passively moved in any way. Moreover, if the patient were given time, he could overcome these attitudes of contracture himself. He could open and close his right hand, flex and extend the fingers, abduct and adduct the same, &c.; in fact, he could make any movement at any joint, but slowly, not strongly, and always to the accompaniment of tremor. He could overcome the habitual position of the lower extremities in a similar way. In spite of the extraordinarily spastic appearance of the face, there was no true contracture of any of the facial muscles or muscles of the throat and neck.

Power.—All voluntary movements executed by the patient were certainly somewhat weak. There was no doubt of this. All could be resisted by the

examiner with comparative ease; the strongest relative movement seemed to be depression of the lower jaw.

In the arms the range of voluntary movement was unexpectedly good, considering the contractures of the limbs. The grasp was better on the left side than on the right; the left biceps was stronger than the right, whereas the right triceps was a little stronger than the left.

All voluntary movements of the legs were relatively better, but not of normal strength. On the whole the flexor groups were weaker than the extensor groups. Adduction at the hip was much stronger than abduction.

In any voluntary movement a jerky action was usually to be observed, when the patient voluntarily adducted his legs it was by a series of jerks, apart from the gross action-tremor which was constantly present. He seemed to be unable to sustain any movement for longer than a few seconds, although encouraged or urged to do so; relaxation began, and once the voluntary effort weakened the affected muscles passed into the ordinary unceasing tremor.

All the muscular groups of the body were tested as far as could be done, and, speaking generally, it may be said that the left side was weaker than the right, and not so tremulous as the right.

Tremor.—Undoubtedly the most striking motor phenomenon in the case was the highly typical rhythmical tremor of the arms and legs. As the patient sat in the sun a ceaseless to-and-fro, up-and-down movement of his extremities at once caught and riveted the attention. This tremor was a beautiful example of a true tremor—i.e., of a rhythmical alternation in contraction of a given muscular group and its antagonists. Its rate varied from four to six a second; it rarely quickened, perhaps, to eight a second. Its range or excursion was also variable; as a rule this did not exceed an inch in the case of the fingers, but with any muscular effort—e.g., in picking out the letters on his alphabet—the range was as much as 3 in. (about 7 cm.). On exertion the tremor became wide and quick; left to itself it was slower and finer.

In the arms the chief tremors were: alternating flexion and extension at the elbow, flexion and extension at the wrist, with the frequent addition of a slight alternating pronation and supination, causing a sort of rotatory tremor; the finger tremor was chiefly flexion and extension, sometimes with the addition of an opposition and adduction element in the case of the thumb. In the legs there was alternating flexion and extension at the knees, though this was of very short range; there was more obvious flexion and extension at the ankles, and most noticeable of all was the tremor of the toes. The lower jaw also, unless the mouth were at its maximum of opening, moved up and down rhythmically through a fine range. When the patient sat up on the edge of his bed there was a distinct to-and-fro movement of the body in an anteroposterior direction.

Speaking generally, the tremor was more noticeable distally than proximally, being in this respect the contrary of the spasticity, as has already been

remarked. When any muscular effort was made the tremor in the corresponding groups increased in degree and rapidity, and often spread; thus by making the patient squeeze my fingers in his hands I could augment the tremor of the lower extremities. With the finger-nose test the tremor was easily aggravated, but there was this difference in the two sides; on the left side the patient put the forefinger to the nose in the usual way, to the accompaniment of a tremor increasing in range, and in doing this the contracture of hand was relaxed, but the right hand in contracture-attitude was always put *en bloc* to the nose.

When it is said that the tremor increased with voluntary action it must be remembered that the patient was incapable of sustaining any voluntary effort for more than a few seconds, hence the increase in the rate and excursion of the tremor was always transient and of brief duration. When the finger or the hand reached the nose the tremor at once became less marked, although the limb was being held in the desired position.

A number of experiments were made to see if by supporting and relaxing all the joints of a limb the tremor would disappear. It was possible in this way, and by quietly encouraging the patient to divert his attention from what was being done, to cause the tremor to cease, *in toto*, for a few seconds. This was effected in the right arm, for instance. When it was left to itself, extended and still, without any interference on the patient's part, the limb almost immediately began to shake again, at first quietly, but with ever-increasing force, and at the same time it began to contract again at the joints, with the result that ere many seconds had elapsed it was back once more in the accustomed position, and shaking as before. The tremor which was the most difficult to cause to disappear was a fine interosseous tremor, coupled with the somewhat rolling tremor of the forefinger and thumb. The involuntary movements were never choreiform or athetoid.

Co-ordination.—No real inco-ordination was to be observed. Even when the tremor was severe, the patient could direct his forefinger to his nose correctly. The occasional irregularity of movement of the eyes could not be called ataxia. There was no static ataxia. When he stood upright, closure of the eyes made no difference to his equilibrium.

SENSORY SYSTEM.

The patient did not complain of any abnormal subjective sensations, and on examination no alteration in any form of cutaneous or deep sensibility could be detected.

REFLEXES.

A slight jaw-jerk was present. The tendon reflexes of the upper extremities were not easy to elicit, because of the tonic condition of the muscles. They were obtained, however, and were equal on the two sides. The abdominal reflexes were present, equal, active, and readily obtainable from all four quadrants. The knee-jerks and Achilles-jerks were brisk and equal; there was no ankle or other clonus. The plantar response was of unmistakeable double

flexor type. In regard to the organic reflexes, the patient was reaching the indifferent stage. His attendant put the bottle to him at regular intervals; if this was not done he passed urine "involuntarily." There was no doubt, however, that he could pass urine naturally; probably his helplessness was sufficient to account for the methods adopted. There was no incontinence of fæces.

GAIT.

This was a very interesting and instructive performance. As the patient was helped to his feet he leant hard on the supporting arm, moving stiffly and clumsily, and ready to fall in any direction, as the maintenance of balance was somewhat hazardous; at the same time there was a perfect riot of tremor. At first he was certainly rather on his toes, but in a short time the heels came down, and with shuffling steps, not unlike a *démarche à petits pas*, he proceeded, tending usually to fall forward. Nevertheless he improved with the effort, and was able to go up and down two steps, and walk along a corridor, slowly, laughing and shaking the whole of the time. He was totally unable to walk unaided.

Such, then, was the condition of the patient when I visited him in June, 1910. During the summer he remained much the same, but towards the autumn, without obvious reason, he began to fail rapidly. He became definitely worse about the beginning of September. Up to that time he had been getting up daily, and sitting as usual in the sun the greater part of the day. He developed an irregular temperature which ran up to nearly 104° F., suggesting possibly some kind of septic absorption. The difficulty of feeding the patient became acute. Slight sores appeared over the heels, trochanters, and sacrum. These were, however, more superficial abrasions than real bed-sores. The tremors of the limbs, especially of the arms, became more violent than ever, and the contractures much more marked. General emaciation rapidly set in. Yet the patient maintained complete consciousness to within a couple of hours of his death. He recognized all those around him, and knew quite well where he was. He was able as usual to express his wants by his alphabet. When asked if he wished anything to drink, he was able, though *in extremis*, to indicate his desires rationally. During these weeks he was incontinent of urine and fæces. He died on the afternoon of September 20, 1910, being then 22 years of age.

RÉSUMÉ OF THE CLINICAL HISTORY OF CASE 3.

A youth of 17, the brother of the patient whose case is No. 2, of normal mental and physical development, active and athletic, breaks down through overwork for an examination, suffers from auditory hallucinations, becomes excited and unmanageable, and is removed to Bethlem Hospital, where a diagnosis of toxic psychosis is made. This

illness is of comparatively brief duration, and the patient makes a complete recovery therefrom, never showing any analogous symptoms at any subsequent period. No signs of organic disease of the central nervous system are noted. In less than a year he is discharged recovered, and appears in good general health.

About four or five months later, the patient being 19 years old, other symptoms of a different nature make their appearance and progress rather rapidly. He begins to have difficulty in speaking and swallowing, and it is noticed that a little saliva escapes from the corners of his mouth. At the same time his hands become tremulous and his handwriting deteriorates. In the course of three months his whole appearance has altered for the worse. The tremor is generalized, his dysarthria is such that he rarely speaks at all; what he says is scarcely intelligible, and he has a constant tendency to keep his mouth wide open. The dysphagia also increases.

In the next year the disease runs a slow downward course. The patient's musculature becomes very stiff, so that his helplessness is considerable; his face wears a constant fixed smile; he is very cheerful, and often breaks into spasmodic laughter; the tremor of the limbs is severe and constant, and increases on exertion; the defect in articulation amounts almost to anarthria. Yet there is no obvious mental impairment beyond a certain childishness which shows itself in the readiness with which he is amused. He is able to read, understands everything that is said to him, indicates his wants, and evidently has a degree of intelligence of which a glance at his physical appearance gives little hint.

From this point the progression of the disease is even more noticeably in a downward direction. When he is just turned 22, about two and a half years from the onset of the illness, and three months before the end, an examination shows the following as the most noteworthy points:—

He has a fixed smile on his face, and bursts frequently into involuntary laughter; his mouth is wide open and the saliva dribbles from it; he cannot swallow, yet his palate moves well and he can protrude his tongue slowly, but completely; he cannot articulate, though he can phonate "ah" fairly well; he can perform upper facial movements well, lower facial movements very badly; there is no nystagmus, and the pupils react briskly to light. He is very thin; his muscles are all hyper-tonic, and he has an attitude of contracture, chiefly flexor, in the arms and legs; yet this contracture can be overcome passively, and also actively, although voluntary movements are very slow; there is no true

paralysis, yet the patient is very helpless, falling and rolling off his chair, owing to the muscular stiffness and weakness combined; his hands and arms, feet and legs, and to a less extent his trunk, show a ceaseless rhythmical tremor, which increases with exertion. The muscular hypertonicity is more marked proximally, the tremor distally. There is no disturbance of sensation. The abdominal reflexes are brisk and a double flexor response is obtained—accepted proofs of the integrity of the pyramidal tracts. With the help of an alphabet he is able to express his wants; he evidently appreciates all that is going on round him; his observation is quick, and he understands everything that is said to him.

Three months later he becomes more acutely ill, his temperature rises, he becomes much weaker, emaciation rapidly progresses, bed-sores and more permanent contractures develop, and, conscious to within an hour or two of the end, he dies, at the age of 22, after an illness of three years' duration.

At no time during his illness, or before, has he shown any of the ordinary symptoms or signs of cirrhosis of the liver.

Case 4.—M. To., aged 20, was admitted to the National Hospital, under the care of Dr. Tooth, on October 20, 1911. She was born on September 19, 1891, and was the third child and only daughter of the following family:—

- (1) Male, died, aged 10, of what is said to have been tuberculous peritonitis.
- (2) Male, aged 22, alive and well.
- (3) Patient (Case 4).
- (4) Miscarriage.

Family history.—Both parents at the time of writing are alive and well. On the paternal side there was a history of "liver" complaints among various members of the family, usually in the form of "headache, sickness, or indigestion." The grandmother on the father's side suffered from jaundice once or twice, but lived to the age of 78. The patient's father had "suffered from his liver" all his life in the shape of "bilious attacks." When he was born his mother was suffering from an attack of jaundice. On the maternal side there was a tendency to "weak chests" among several members of the family.

Previous history.—The patient was never very strong, but, on the other hand, had had no serious illness at any time. About five years before coming under observation she had a moderately acute attack of jaundice, which lasted rather more than three weeks. No ill-effects followed this illness apparently, nor did the icterus return. From that time the patient had never shown any symptoms referable to disturbance of the liver. Menstruation was established at the usual age, and was regular up to the commencement of the present illness more than a year ago, since when the patient had menstruated only

twice, on each occasion losing a large quantity. Since the age of 18 she had become very tall.

History of present illness.—About the month of May, 1910—i.e., about one and a half years before the patient entered hospital—it was remarked that her handwriting was not quite so good as it had hitherto been, and that there was an almost imperceptible tremulousness of the right hand. A few months later this tremor of the hand became definitely noticeable in the performance of fine movements, such as needlework, and about the same time the right lower extremity was also occasionally seized with slight tremulousness. From its onset the tremor of the right limbs steadily progressed. It was at first considered that the condition was functional, and a Weir-Mitchell rest cure of some weeks was carried out, but without much result. In addition to the tremor the patient presented certain indications of pulmonary weakness, but although this condition responded well to treatment and eventually disappeared, the nervous symptoms remained. About a year ago her parents noticed that the patient's voice was becoming a little husky, and her articulation a little indistinct. About six months before her admission to hospital definite dysarthria and dysphagia made their appearance, and these symptoms, too, progressed without remission. The patient used to be fond of going long walks, but since that time her legs became weak and stiff; she could only take short walks, and tired readily. In the course of a month or two she found herself unable to walk without strong support. Within the last three months the left hand and arm started to tremble, but not so constantly or so severely as on the right. It was frequently remarked that with any attempt at voluntary movement of the right limbs they were thrown into tremors, and observing this herself, the patient took to shaking hands with her left hand instead.

During the last six months the difficulty in swallowing and in mastication had been such that the patient could not bite satisfactorily, and was unable to swallow anything but fluids, or bread and butter. The latter was pushed to the back of the throat before she could swallow it. The dysarthria gradually degenerated into complete anarthria. The end syllables of words were slurred over, until her speech became unintelligible. Occasionally, in the mornings, the patient was still able to articulate a few words more or less clearly. It was noticed that sometimes the patient's lips and tongue moved as though to form a word, but no phonation was accomplished.

During the three months prior to her admission to the National Hospital, the symptoms above enumerated all increased in severity. In addition, contractures of the limbs appeared, more particularly on the right side. The limbs became stiffer and more difficult to move, till at length the patient could not completely extend her right wrist or fingers. With this rigid condition of the muscles they began also to waste, no doubt in part as a sequel to inadequate nutrition, and when the patient came under notice she was very thin indeed. There was, however, no special wasting of any particular muscle or group of muscles, if exception be made of the fact that the right shoulder muscles were perhaps thinner than on the left side. Her face was

expressionless and fixed in a mask-like tonic contraction, the mouth being constantly held open, while saliva slowly dribbled from the corners. Any effort at articulation resulted in the appearance of tremors in the neck and trunk, especially if the effort was sustained. There was often a fixed smile on the patient's face, but exaggerated emotionalism was not conspicuous, nor was there a true "rire spasmodique." Her mental condition throughout appeared to be quite satisfactory. She read novels with avidity; took an intelligent interest in topical events; was correctly oriented in time and space, and suffered from no abnormal condition such as delusions or hallucinations.

During the last few weeks there had been some difficulty in passing water, which was relieved by the application of hot fomentations. There had been, also, a good deal of constipation.

Condition on admission.—The patient was a very tall and thin young woman. Her height was about 6 ft. 2 in., but she did not weigh more than 8 st. There was no sign, subjective or objective, of pulmonary mischief. The urine, of specific gravity 1015, contained a few pus-cells microscopically.

She looked bright and intelligent, in spite of the vacant facies; with her eyes she followed the events of the ward with quickness and alertness, and it was clear she was fully cognizant of all that was done for her and of the details of the examinations to which she was subjected. All questions were answered to the best of her ability, by gesture or otherwise, and all requests were obeyed with readiness. In the appreciation of written and spoken language there was no defect whatever. No explosive laughter was noticed, yet the patient was probably a little more emotional than normal. The contrast between the opened, fixed mouth, with saliva dribbling over the chin, and the peculiarly lively expression of the eyes, was remarked by all who observed her.

When the patient laughed some sound came from the throat, otherwise phonation was practically absent. It was odd to note the emission of this scarcely recognizable sound from an immobile face. Articulation was also almost absent. She could make sounds approximating to "yes" and "no" in a whisper, also certain other words which those who knew her best were occasionally able to determine.

She complained of nothing in particular; was not in pain; and at the same time gave no definite indication of mental distress at being unable to express herself.

CRANIAL NERVES.

Visual fields, vision, and optic discs were all normal.

The pupils were equal, regular, of medium size, and of normal reaction in every way. The ocular movements were normal. There was no nystagmus in any direction.

The mouth could be opened to its full extent, but the patient was unable to bring the teeth firmly together. Lateral movements of the inferior maxilla were very imperfect. Biting and chewing were impossible.

There was no defect of facial sensibility. The corneal reflex was brisk on both sides.

The more or less constant facial expression of the patient is seen in fig. 23. The upper teeth and a good part of the upper gums were always visible; the corners of the mouth were retracted in a stiff and rather fatuous smile; with the exception of slight play of the eyelids, expressing pleasure or otherwise, the facial musculature was rigid and immobile. She could not whistle, but could slowly purse up her lips to form a more or less circular opening. The eyes could be opened and shut with some power.



FIG. 23.—M. To. (National Hospital, October, 1911). Characteristic fixed smile and retracted lips. Note intelligent expression of eyes. The patient is falling stiffly to the right.

Hearing was normal on both sides.

The dysphagia and anarthria have already been referred to. In spite of the anarthric condition the patient's soft palate rose fairly well and symmetrically on the effort to phonate. The palatal reflex was brisk from either side.

The sternomastoids were in a state of hypertonicity, and did not relax though the patient was reclining. The head could be rotated slowly from side to side, to the accompaniment of tremor of the head and trunk.

The tongue, though rather thin, was not atrophic, and showed no sign of fibrillation, nor was it puckered or fissured. It could be protruded slowly,

and in a straight line, but only for a short distance. Lateral movements of the tongue were not so good.

MOTOR SYSTEM.

The musculature throughout was very thin, the wasting being generalized. No fibrillation was detected. The case presented the characteristic motor symptoms of tremor, rigidity, and contracture, and these may be described in turn.

(a) *Involuntary movements.*—The right arm and leg were in a state of continuous clonic tremor—a regular rhythmical involuntary movement affecting all the joints of the limbs, and not, in this case, more marked distally than proximally. The excursion was wide and the rate rather quick, about three or four a second. During the waking hours it was never absent. With excitement or exertion it sometimes became violent, the right leg and foot striking the bed in a rapid succession of rhythmical alternating flexion and extension movements, mainly from hip and knee. Unless the right arm were held by the side its tremor became coarse and severe. A similar tremor was present in the left limbs, but here, while of the same regular and alternating type, it was certainly less pronounced and sometimes scarcely to be detected. Further, voluntary control over the tremor of the left half of the body was less impaired than over the right. With strong muscular effort against resistance the tremor always exhibited a tendency to become generalized in head or trunk, or to spread to the lower extremity when the upper was prevented from carrying out a given movement. There was less tremor of the interosseous and small-hand muscle type in this case than in the others which I have observed, but occasionally such involuntary movement could be seen. The movements of the limbs were never choreiform or athetoid.

(b) *Rigidity.*—The right arm and leg, and to a less extent the left, were in a state of hypertonicity, which, as far as the former are concerned, could only be described as extreme. Fig. 24 gives some idea of the general attitude of the upper extremities. The right arm was flexed at all joints, with the exception of the terminal joints of the fingers. So great was the flexion at the wrist that the fingers almost touched the middle of the forearm. The right leg was in extensor spasm, the foot being in a somewhat equinus position, and the right great toe slightly dorsiflexed. On the left side the arm and leg were in more or less analogous positions, but the spasticity was not quite so great, although evident enough. Everywhere the musculature was firm and hypertonic. Of this one could easily convince oneself not merely by palpation but by impressing passive movements on the various segments of the limbs, when it at once became obvious that whether the movement were one of extension or of flexion the antagonists were in each case equally resistant to the movement. As the patient lay in bed the generalized spasticity of the musculature gave the patient the appearance of being, as it were, "soldered," an impression the effect of which was heightened by the slowness of her voluntary movements. When she stood upright, her feet together, she always tended to fall "like a

pillar," indifferently in any direction. The abdominal muscles were peculiarly tense and firm, and never relaxed. The trunk moved *en bloc* when the patient endeavoured, on request, to bend her body forwards or backwards.

(c) *Contracture*.—Definite contracture had set in at various joints—a true contracture, which could not be overcome by passive movement. It was impossible to raise the right arm beyond a right angle at the shoulder; at the elbow the arm could not be quite completely extended. The forearm could not be put into a position of full supination. The flexion at the



FIG. 24.—M. To. Note characteristic contracture-attitudes, tremor of right hand (the patient is grasping her nightdress with that hand in the endeavour to keep the limb as steady as possible), open mouth, vacant expression.

wrist could only be undone to a slight extent. The skin on the anterior aspect of the right wrist was raw as a result of the continued flexion. The right leg could be bent up fairly easily; passive flexion and extension at the various joints were not materially interfered with. On the left side the condition was one of "contracture attitude," without true contracture. Thus at all joints passive movements were possible, and could be carried out completely, although the limbs appeared to be in as extreme contracture as those of the opposite side.

(d) *Voluntary movement.*—There was no doubt that voluntary movements were weak, apart from the spasticity and contracture. The patient could extend the right arm at the elbow to about a right angle, but not further. When the right fingers were passively unbent she was able to grasp fairly well. She was unable voluntarily to overcome the contracture at the right wrist. Voluntary movements of the right leg could be effected at all joints, but they were weak and slow. Similarly the left arm and leg could be used voluntarily at all joints, but again in a slow and stiff fashion. There was no paralysis in the real sense of the word, for the patient could innervate and actuate voluntarily all her muscular groups; where no movement occurred the displacement of the segment concerned was prevented by contracture, not by paralysis.

No inco-ordination or ataxia was discoverable.

The patient could walk slowly and stiffly, but quite steadily. She stood upright without swaying if the feet were a little apart. Closure of the eyes caused no unsteadiness.

SENSORY SYSTEM.

No change in sensibility was present. All the usual tests for sensation were utilized in the examination.

REFLEXES.

The arm-jerks were brisk, a little more so on the right than on the left.

The abdominal reflexes could not be obtained owing to the great rigidity of the abdominal muscles. The knee-jerks were present and equal, not exaggerated. The ankle-jerks were present and equal. There was no clonus. The left plantar response was flexor; the right, more difficult to obtain, appeared to be flexor. The function of the organic sphincters was normal.

The only other point to be mentioned in the examination is that there were no indications of liver disease; there was no œdema, no ascites, icterus, or distended veins. The liver reached from the fourth intercostal space to 1 in. (2.5 cm.) above the costal margin—i.e., 5 in. (about 12 cm.) in the right mammillary line.

RÉSUMÉ OF THE CLINICAL HISTORY OF CASE 4.

A girl, aged 18, who had an attack of jaundice some four or five years previously, but whose mental and physical development has been up to the normal standard, is noticed to develop a certain tremulousness of the right hand, so that her writing deteriorates, and she is somewhat awkward in the performance of fine movements with the fingers. A few months later the right leg begins to show some shakiness, and at the same time articulation becomes a little defective. So slight are the signs, however; that a rest cure is undertaken in the hope that the condition will thus clear up. But the symptoms steadily progress,

and definite involvement of the nervous system can no longer be denied. The limbs very gradually become stiff, more especially on the right side, and walking becomes more difficult; certain contractures appear in the right arm. As a result of an increasing dysphagia, which is associated with the dysarthria, the patient gradually emaciates, though there does not appear to be any local wasting of muscles. Within a year and a half of the onset of the disease she has become completely anarthric; her muscles have become extremely hypertonic both in trunk and limbs, yet her voluntary control over them is very fair; the upper extremities are fixed by contracture in the attitude of flexion, there being a true contracture on the right side, but only a "contracture-attitude" on the other, for the patient is still able to move that limb at all the joints. Along with the hypertonicity and contracture there is a never-ceasing rhythmical tremor of the limbs, sometimes also of head and trunk, coarse in type, and sometimes violent, which is more noticeable on the right side.

Examination shows that the pupil-reflexes are normal; the optic discs are normal; there is no nystagmus; there are no sensory changes; there is no clonus at the ankle, and a flexor plantar response is obtained on the left side, and with some difficulty, owing to contracture, on the right. There is no sphincter impairment. It may be said, therefore, that the so-called "signs of organic disease" of the pyramidal system are wanting, but the anarthria, dysphagia, tremors, spasticity, and contractures present a clinical picture indicative of a profound disturbance of motility. The face is immobile; the corners of the mouth are retracted in a spastic smile; saliva runs from the lips; the mouth is widely open; only the lively and interested expression of the eyes remains to show that the patient's mental condition is one of alertness and intelligence. There are no indications at all of hepatic disease.

Case 5.—Samuel M., the eldest member of the M. family, was born in 1864, and was quite well as a child. He developed in a normal manner, physically and mentally, and was in good health till the age of 9. At this age he accidentally fell into the Regent's Canal, and soon after developed typhoid fever. It was a severe attack, lasting, with relapses, over the better part of six months.

Rather less than a year later, when he was 10 years old, it was noticed that his fingers and hands were beginning to shake when he used them in any muscular effort, and that he could not walk properly. His gait began to be somewhat shaky. The condition gradually got worse. About a year or so from the commencement of the illness he began to suffer from an articulatory defect and swallowing became difficult. In the course of another year the

extremities became contracted, and he had to be fed and nursed by others owing to his helplessness. He used to keep his mouth open and to "make a groaning noise." He was admitted to the National Hospital some time in the year 1878, but the notes cannot be found. He was discharged unimproved and taken home, where his condition steadily deteriorated. He was "reduced to skin and bone," and so helpless that "he could not move hand or foot." Anarthric, dysphagic, emaciated and contractured, he lay in bed with all his limbs "constantly on the work." He died in 1879, aged 15 years all but a few days, after an illness of about four and a half years' duration.

Case 6.—Christopher J., aged 13, was admitted to the National Hospital, Queen Square, under the care of Dr. Thomas Buzzard, on January 18, 1889, with the following history:—

Two years before, for no obvious reason, the boy began to have difficulty in walking; he dragged his feet along the ground instead of lifting them properly, and his feet began to turn in slightly. About the same time he had to leave the choir in which he sang owing to "loss of voice." It was not that his voice broke, but he could not phonate properly.

A few months after the commencement of the illness some discoloration of the lower extremities was noticed. Bright purpuric spots appeared on the skin and faded gradually. At intervals since that time, crops of these spots appeared. There was no fever, but the joints were sometimes slightly swollen. Since then, the patient gradually became weaker on his legs.

About thirteen weeks before his admission he had œdema of the legs and scrotum, and some ascites. These symptoms improved. About a month before admission he had some difficulty in controlling the action of his sphincters. Formerly he was a bright and intelligent boy, in the sixth standard, but since the illness commenced he became duller and more stupid, noticeably so during the last month.

The patient was an only child; the parents were perfectly healthy, and the mother had had no miscarriages.

On admission he was seen to be pale and rather delicate-looking. His mental condition was striking; he was very emotional, at one time laughing, at another crying. He was slow in answering questions, and the saliva often dribbled from his open mouth. He was slow in understanding what was said to him, but did everything correctly that he was asked to do. There was some general wasting of the musculature, most evident below the knees, and there was some contracture at the ankle, as the patient was unable to move that joint, or only to a very little extent. The toes were in a state of more or less constant rhythmical tremor. Passive movements at the ankle were not easy of execution, and caused the patient pain, though not of any severity. He could move the legs well, but less well distally than proximally. The deep reflexes in the legs were increased, and there was a tendency to ankle-clonus on both sides. The plantars were "brisk."

In the arms all movements could be carried out, but were undoubtedly weaker than normal. The arm reflexes were active and equal. The abdominal

and epigastric reflexes also were brisk, and equal on the two sides. The pupils, optic discs, and ocular movements, were all normal.

The illness progressed rapidly; the boy's emotional state became aggravated; he laughed or cried on the slightest provocation. His legs became more contracted, and were constantly drawn up at the knees and hips. Constant sudden involuntary movements of the lower extremities occurred; they were abruptly drawn up and rather more slowly relaxed. The arms in their turn became rigid; the left arm began to contract up, and there were sudden involuntary alternating movements of pronation and supination to be observed. The same thing was noticed in the right arm, to a less extent.

Edema and ascites set in and on February 14 the child died.

If we summarize this case briefly, its salient features are as follows:—

A little boy, aged 13, who has always been healthy and intelligent, begins to have difficulty in walking, and his voice alters; he becomes gradually more emotional, laughing or crying at the merest trifle; his mouth is open and saliva dribbles away; his muscles waste and become rigid, and then the extremities contract, the legs first, and later the arms; there is rhythmical tremor of the feet and toes, and attacks of involuntary spasmodic movements in the upper extremities, usually of an alternating type (pronation and supination, flexion and extension); he loses control over his sphincters. The abdominal reflexes remain brisk, however—a significant fact. Emaciation sets in, and he dies after an illness of about two years' duration.

He has shown very definite signs at intervals of defect of liver function, but there is no evidence of congenital syphilis.

CHAPTER III.—PATHOLOGICAL FINDINGS IN THE PERSONAL CASES.

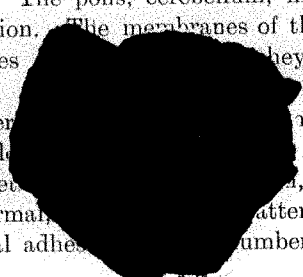
In this chapter is given the complete pathological examination of three personal cases of progressive lenticular degeneration whose clinical history has been given in the previous chapter. In addition, there is a brief account of the pathological findings in Case 6, that is to say, the case referred to in the paper, the details of which have not hitherto been published. In Case 5 there was no pathological examination.

The harmony in the pathological findings of the personally observed cases is no less convincing than the similarity in their clinical features. It is true that the pathological investigation of Case 2 is not as complete as I should have liked, but there is ample evidence that its place with the others is beyond cavil. Cases 1 and 3 are identical,

pathologically, except that the latter is not so advanced as the former. It is, in fact, a fortunate circumstance that the degree of pathological change is not so great in Case 3, for clinically the patient was almost as profoundly affected as the patient whose case is No. 1. By this means what pathological change to associate with the clinical symptoms can be more readily determined, and due reference will be made to this important point in a subsequent chapter.

There are certain features of the pathology of the three personal cases which may very briefly be emphasized by way of introduction. In the first place, there is no pathological evidence that the cases are syphilitic; in fact, syphilis may be excluded pathologically, as I believe it can be clinically. The two earlier cases were under observation in pre-Wassermann days, while in the third case I had no opportunity of applying the test. Secondly, there is no pathological evidence that the disease is congenital, nor are there anomalies of development of any kind. Thirdly, the pathology furnishes proof that a selective morbid agent of a peculiar and perhaps unique kind must have been at work.

Case 1.—The autopsy was performed by myself at 9 p.m. on the evening of Wednesday, July 29, 1908, twenty-five hours after the death of the patient, in hot weather. The body was greatly emaciated, and rigidity was profound, but there were no bed-sores or abrasions. *Post-mortem* lividity was pronounced.

On opening the calvarium the dura was neither adherent nor discoloured; its veins and sinuses were engorged, but otherwise normal. The subarachnoid spaces and cisterns were greatly distended with cerebrospinal fluid. The arachnoid was observed to be somewhat "milky" at the base of the brain, in particular across the interpeduncular space. The arteries at the base presented no visible abnormality. The pons, cerebellum, medulla and cord seemed normal on a rapid inspection. The membranes of the cord were not thickened. As the cranial nerves  they appeared to be normal.

The brain and cord were immersed in formalin. They were weighed the next day, with the following results: Brain, complete, 1,350 gm.; cerebellum, medulla, and pons, together, 1,204 gm.

The heart and lungs were normal. The lungs were somewhat congested. There were old pleural adhesions, most numerous, on the left side posteriorly.

The liver, when removed from the abdomen, presented a very striking appearance, seen in figs. 25 and 26. It was intensely cirrhotic; the whole of its surface was covered with irregular rounded nodules of liver-tissue, about the size of small hazel-nuts, surrounded by bands of connective tissue, of

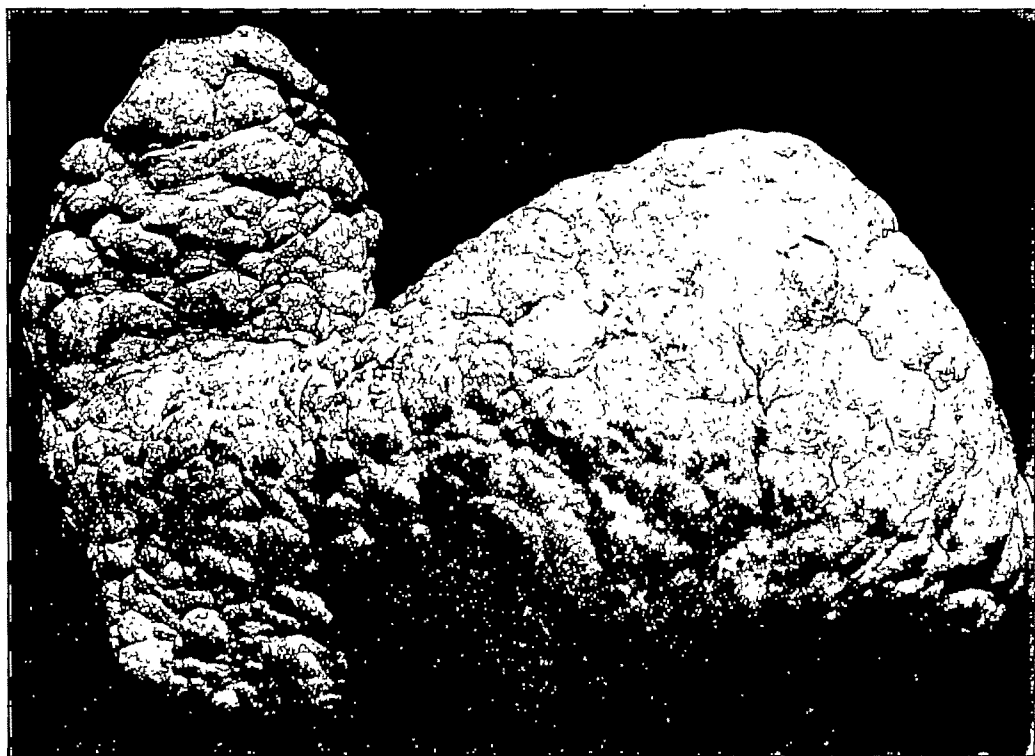


FIG. 25.—Liver (S. T., Case 1), from above.



FIG. 26.—Liver (S. T., Case 1). Transverse section.

varying width. Some nodules were considerably smaller. The capsule of the liver was not obviously thickened, except in one or two places. There were no adhesions to the neighbouring viscera. The organ was not bile-stained, and was perhaps rather lighter in colour than usual. On making a transverse incision through it, it was seen to be cirrhotic from one side to the other; it was divided up into nodules varying in size from a shilling to a threepenny-piece, or less, between which was a great deal of connective tissue overgrowth, sometimes of considerable width, especially in the deeper parts of the viscus. There was much thickening along the portal tracts. The cirrhosis was mainly multilobular.

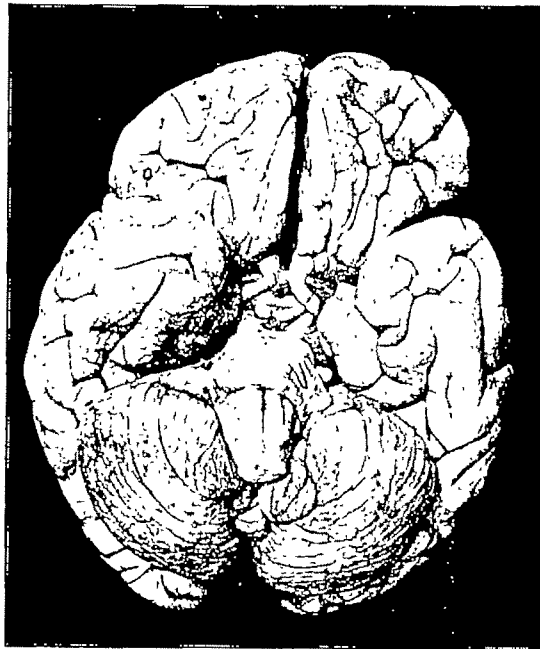


FIG. 27.—Basal surface of brain (S. T., Case 1).

The weight of the liver and gall-bladder was 1,380 grm. It was very firm and preserved its shape. The gall-bladder did not show any abnormality.

The spleen was not obviously enlarged; it was firm and rather congested, and its cut surface on section seemed normal.

The kidneys were normal.

The pancreas and the intestines were unaltered. The stomach was three-parts full of dark liquid blood; its mucosa was greatly congested, but no ulceration was discovered, and a rapid search for a ruptured vessel or vessels was unsuccessful.

There was no ascites.

The suprarenal on the left side, pieces of the following muscles—right thenar eminence, left biceps, left flexor sublimis digitorum, left extensor communis—together with a piece of the left lobe of the thyroid, were taken for subsequent examination.

MACROSCOPICAL EXAMINATION OF THE BRAIN AND CORD.

After hardening in formalin the brain was stripped of its membranes. These were not adherent anywhere. Pieces of the middle cerebral artery and its branches were taken for microscopical investigation.

The cerebral hemispheres were well developed and did not show any atrophy or undue spacing between the convolutions. The pattern of the latter was normal (figs. 27 and 28). In particular the frontal lobes were not the

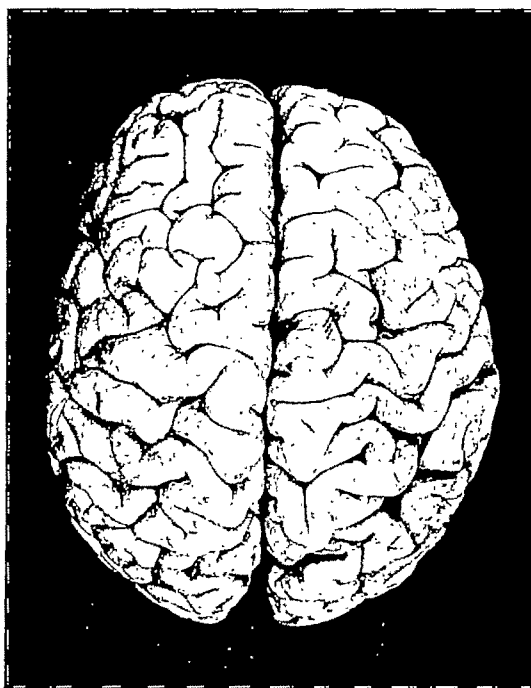


FIG. 28.—Upper surface of brain (S. T., Case 1).

seat of any obvious naked-eye pathological change. The corpus callosum was divided in the mesial plane, when the mesial aspect of the hemispheres was examined and found to be normal.

Each hemisphere was then cut across by Pierre Marie's *coupe d'élection*, a section which passes under and just touches the extremities, anterior and posterior, of the corpus callosum as it appears on the mesial aspect, and is

carried horizontally outwards to the lateral aspect of the hemisphere. When this was done the picture reproduced in fig. 29 was revealed.

The eye was at once caught by a remarkable bilateral and symmetrical cavitation of the lenticular nucleus; its severity in degree seemed the more

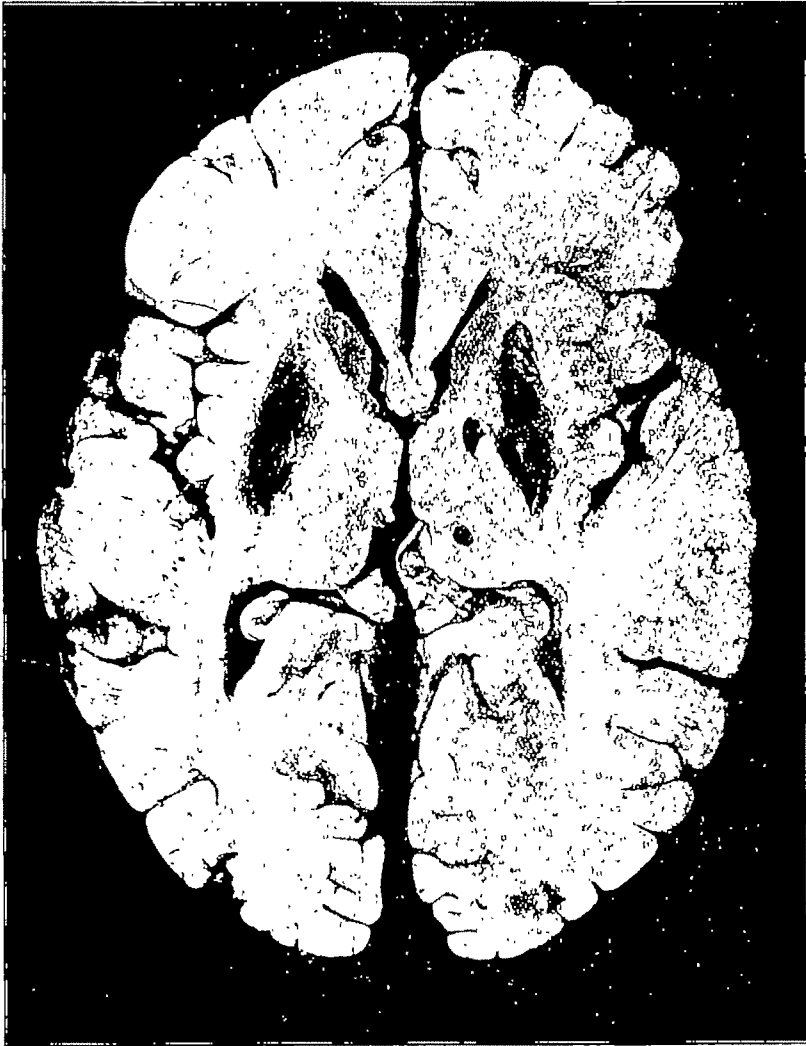


FIG. 29.—Horizontal section through hemispheres (S. T., Case 1). (They are reversed in the figure, the left being at the right-hand side.)

astonishing since the rest of the cut surface of the hemisphere was normal. The cortex and the white matter of the hemispheres did not present any abnormality; the thalami were of good size and shape; the internal capsules stood

out clearly (with an exception, to be noted immediately), but the putamen and globus pallidus had almost entirely disappeared, and in their place on each side was a crumbling cavity.

Right side.—Almost the whole of the right putamen, with the exception of its anterior fifth, and the globus pallidus, with the exception of its extreme inner part, were destroyed, while the small sections that remained were soft and disintegrated. In their place was a cavity lined with irregular dirty brown tissue débris, which subsequent examination showed to extend from the upper to the lower limit of the lenticular nucleus. Its greatest dimensions were $2\frac{1}{2}$ cm. long by $1\frac{1}{4}$ to $1\frac{1}{2}$ cm. wide. It did not contain any fluid. The outer margin of the cavity was formed by a steep wall which corresponded strictly to the outer aspect of the nucleus, and was sharply differentiated from the claustrum and island of Reil convolutions, which, although subsequent microscopical examination showed they were slightly degenerated, certainly did not present any sign of loss of substance. Posteriorly the cavity came to an end at a point corresponding to the posterior end of the nucleus, while its inner wall was formed by the internal capsule, except at the anterior part, where a little piece of globus pallidus tissue remained.

The external capsule in its middle third was thinned and had undergone loss of fibres. The caudate nucleus was somewhat shrunken, but compared with the destruction of the lenticular nucleus it was well preserved, and its fine fibres could be easily distinguished.

The internal capsule was untouched, though it looked rather undermined in one place; its anterior and posterior limbs looked perfectly normal. A few fine internuncial fibres from the extreme anterior part of the putamen, running mesialwards, could still be seen. The optic thalamus was to all appearance normal. The rest of the section presented no visible morbid appearance.

Left side.—The cavity formation on the left side was almost identical with that on the right. It was, however, even more severe. It occupied the whole of the lenticular nucleus, with the exception of a small portion of the globus pallidus anteriorly and to the inner side. It extended right back to the point at which the nucleus came to an end. On the outer side the cavity had destroyed part of the external capsule, at the junction of its middle and posterior thirds, and had extended into the claustrum slightly. Anteriorly, on this outer side, the crumbling débris of the nucleus had fallen away from the "bed" in which the nucleus lay, leaving a clean-cut edge to the cavity which is well brought out in the figure. On the inner side the cavity had undermined the internal capsule at its genu, and a small extension from the main part had made its way across the capsule, separating but not destroying the fibres, at least not to any extent, as will be seen later.

The cavity walls were highly irregular, and dark brown in colour; the débris that was left was soft and granular. Subsequent investigation showed that on this side also the cavity occupied almost the whole extent of the lenticular nucleus in a vertical direction. In one or two places thin strands of shreddy material still bridged it across, more particularly towards its

anterior end. Its dimensions were $2\frac{1}{2}$ cm. long by $1\frac{1}{2}$ cm. broad. The diameter of the little prolongation of the main cavity across the internal capsule was 7 mm. There was no brownish slough in this little subsidiary cavity, and no sign of softening round it.

The anterior limb of the internal capsule was normal. At the genu was the cavity prolongation already described. The posterior limb of the internal capsule looked quite normal, though it appeared somewhat undermined by the cavity; the retrolenticular segment was normal.

As on the right side, the caudate nucleus seemed rather small, and less rounded than usual, but it was not softened; in fact, it appeared well preserved and its internuncial fibres stood out prominently. The latter had all disappeared from what was left of the globus pallidus on this side.

The optic thalamus contained towards its posterior and inner side a small shallow, almost circular, depression, like a little punched-out hole, which was sharply defined, had no softening round it, and was not connected with the main cavity. Its diameter was 3 mm. Otherwise this ganglion was normal to all appearance; it was not atrophic or shrunken in any way.

The convolutions of the island of Reil did not show any obvious loss of substance.

The rest of the section presented no visible morbid appearance.

There was no internal hydrocephalus, and no ependymitis. The whole of the visible cortex on these sections appeared of good depth.

The spinal cord seemed, on naked-eye investigation, to be of normal appearance. Its transverse sections, at various levels, were of good size, and did not show any trace of degeneration. The membranes were not obviously thickened, unless it were that the pia-arachnoid was a little "milky," chiefly along the posterior aspect of the cord.

MICROSCOPICAL EXAMINATION OF THE NERVOUS SYSTEM.

(1) *Muscles*.—Sections were stained by the following methods: Hæmatoxylin-eosin, hæmatoxylin-Van Gieson, Weigert-Pal for intramuscular nerves, counterstained with eosin.

Speaking generally, the muscle-fibres were all of good size, and all about the same size; there was no disparity in this respect. There were no hyaline changes, no splitting of fibres, no loss of longitudinal or cross striation. What was chiefly remarked was a frequent change in the contour of the fibres, whereby they became more rounded, and less polygonal or polyangular than usual. In addition to this change, the muscle-fibres were often less closely packed together, and a degree of commencing interstitial change was frequently observed.

In some places the sarcolemmal nuclei were much increased in numbers. The muscle-spindles were normal, and no change was discovered in the intramuscular nerves.

(2) *Peripheral nerves*.—These were not separately examined.

(3) *Spinal cord*.—The histological methods utilized were: Weigert, Weigert-Pal, Nissl, hæmatoxylin-eosin, hæmatoxylin-Van Gieson.

(a) *Fibres*.—A glance at figs. 30 to 32, from sections stained by Weigert's original method, will show that there was no systematized degeneration in the cord. The white matter everywhere stained well. The pyramidal tracts were normal throughout, and stained deeply and equally. There was no shrinkage of the white columns, although there was a trace of marginal loss of fibres.

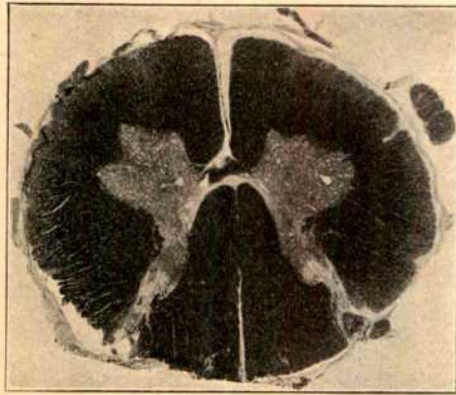


FIG. 30.—Cervical cord (Case 1). Weigert.

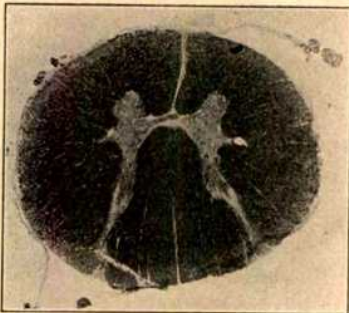


FIG. 31.—Dorsal cord (Case 1). Weigert.

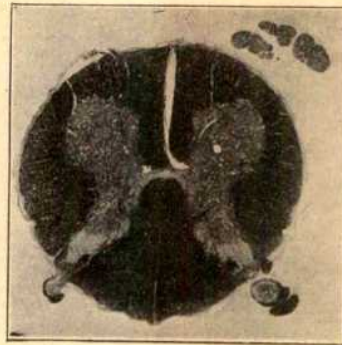


FIG. 32.—Lumbar cord (Case 1). Weigert.

The fibres of the grey matter also stained well, and were not apparently reduced in number. The integrity of the pyramidal paths in the cord is a significant fact in view of the complete motor helplessness of the patient, and of the contractures, tremors and hypertonicity.

(b) *Cells*.—These were carefully examined at various levels (fig. 33). In the first place they were present in good number, and preserved their normal

grouping. The majority, in both cervical and lumbar enlargements, were of good shape and staining reaction. A number, however, were rather elongated, and stained more deeply than usual, apparently owing to some shrinkage of the achromatic part of the cytoplasm, whereby the tigroid elements were brought more closely together, thus rendering the hue of the cell darker. Such cells retained their nucleus, and there is no reason to suppose that they had lost their function completely. Cells of this type are often met with in chronic diseases of the nervous system, in which the patient has not the full functional use of his limbs. Other cells, much fewer in number, showed commencing

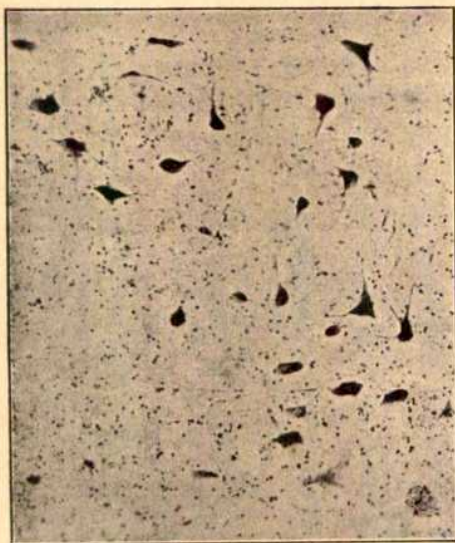


FIG. 33.—Anterior horn-cells, cervical region (Case 1). Nissl.

pigmentary degeneration. Others showed the changes that are associated with a more acute degenerative process—viz., pulverization of the chromatin elements round the nucleus, excentricity of the latter, and disappearance of its membrane. Such cells usually appeared somewhat swollen. In this case their presence may be indicative of a terminal infection.

On the whole, the actual numbers of the anterior horn-cells were apparently slightly reduced compared with a healthy—i.e., normal—cord.

(c) *Meninges*.—There was slight pial thickening round the cord, more especially in the cervical region. It is important to note, however, that small-cell infiltration was entirely absent. Neither in the meninges nor round the spinal vessels was there any trace of inflammatory reaction. The spinal vessels themselves were normal; they were not thickened in any of their coats, nor could anything approaching endarteritis be discovered. The intramedullary vessels similarly were healthy.

(4) *Medulla oblongata and pons*.—The same methods were utilized for these as for the examination of the cord.

With the Weigert-Pal stain for medullated fibres no change could be detected (fig. 34). The pyramids stained normally, and were not apparently

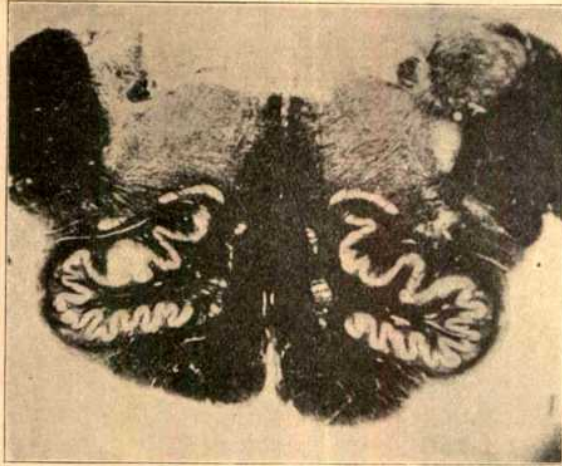


FIG. 34.—Medulla (Case 1). Weigert-Pal.



FIG. 35.—Hypoglossal nucleus, right side (Case 1). Nissl.

atrophic; they did not appear to have undergone any gross loss of fibres. In the position of the descending mesencephalo-spinal tracts no defect could be found. The olives, restiform bodies, fillet, &c., were to all appearances normal.

The cells of the motor cranial nuclei were investigated by Nissl's method. Fig. 35 shows the appearance of the cells of the right hypoglossal nucleus. It will be seen that there was no obvious loss of cells, distinguishing the condition at once from an ordinary bulbar palsy. Many revealed that alteration which has already been noted in some of the cells of the anterior horns—i.e., they were drawn out, stained more deeply, and were less easy to differentiate structurally, but retained their nucleus. The processes of the cells were elongated and often rather more wavy than usual. Examination of the nucleus shows that the "uselessness" of the tongue during life was not due to any atrophic paralysis.

The cells of the other motor cranial nerve nuclei examined were found to be similar to those just described.



FIG. 36.—Crus cerebri (Case 1). Weigert-Pal.

(5) *Cerebellum*.—From the structural point of view, as regards both cells and fibres, this organ was normal.

(6) *Crus*.—Weigert and Weigert-Pal sections of the crus cerebri were made. Fig. 36 shows that the pyramidal tract and the components of the crura on either side of it were unaffected. A little higher up it can be seen that some of the fibres constituting the corticobulbar and corticopontine paths ("faisceau geniculé") which lie on the mesial side of the pyramidal path proper, are partly degenerated, as a result of the lesion at the genu of the internal capsule (left hemisphere). (See fig. 29.) The fibres and cells of the substantia nigra were possibly somewhat impaired, but there was no whole-

sale disappearance of these structures. The tegmentum generally was quite intact. The fibres of the red nucleus were apparently normal; they stained well, as can be seen in fig. 36, and the nucleus was of good size.

The cells of the red nucleus were examined with Nissl's method, as well as with hæmatoxylin-Van Gieson. They did not seem to be abnormal in any way, although it was noticed that a number of them were immediately surrounded by parasite glial cells, but not to a great extent.

(7) *Basal ganglia, internal capsule, subthalamie region.*—The two hemispheres were subjected to a complete examination by the method of serial sections. The right hemisphere, with the exception of the frontal and occipital poles, was cut up into slabs, 1 cm. thick. These were cut exactly at right angles to the *coupe d'élection*, and eight such slabs were impregnated with Müller's fluid, embedded and cut in celloidin, in complete series from before backwards. Every fourth section was stained either by Weigert's original stain or by Pal's modification. (See fig. 37.)

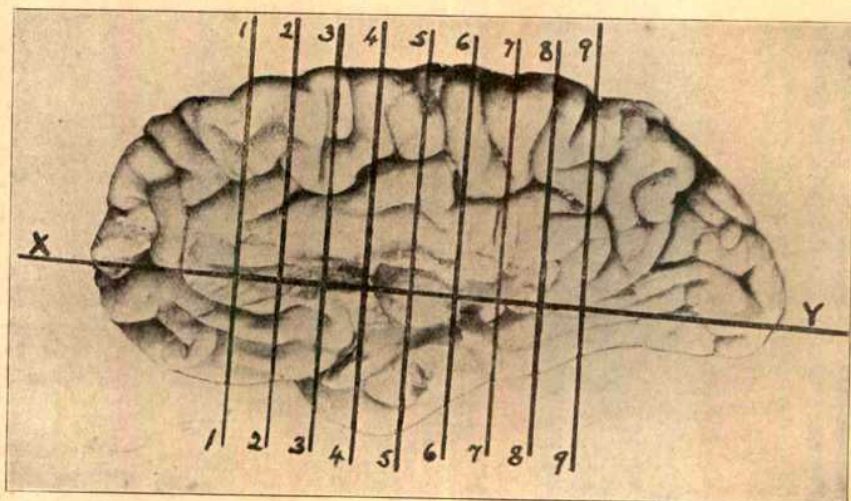


FIG. 37.—Shows method of subdividing the right hemisphere (Case 1) for examination in serial section. Each block is 1 cm. thick. x—y is the line of Marie's *coupe d'élection*.

On the left side the hemisphere, with the exception of the frontal and occipital poles, was divided by a number of incisions exactly parallel to the *coupe d'élection* into a series of slabs 1 cm. thick. Of these, two were above the plane of the *coupe*, and two below. Fig. 38 shows their position in relation to the mesial aspect of the hemisphere. They were impregnated with Müller's fluid, embedded in celloidin, as in the case of the other hemisphere, and cut in complete serial section from below upwards. Each fourth section was taken, and stained as above.

Figs. 39, 40 were obtained when the right hemisphere was cut into divisions.

The first of these represents the naked-eye appearance of the anterior aspect of the slab at the line 4—4, and the second at the line 5—5 (of fig. 37). They portray, in a striking manner, the specificity of the lesion in progressive lenticular degeneration. They demonstrate the integrity of the optic thalamus, the relative integrity of the caudate nucleus, and the complete cavitation and destruction of the lenticular nucleus. The posterior end of the cavity, looked at from the front, as seen in fig. 40, is a striking object; the curious limitation of the lesion could not be brought out more convincingly.

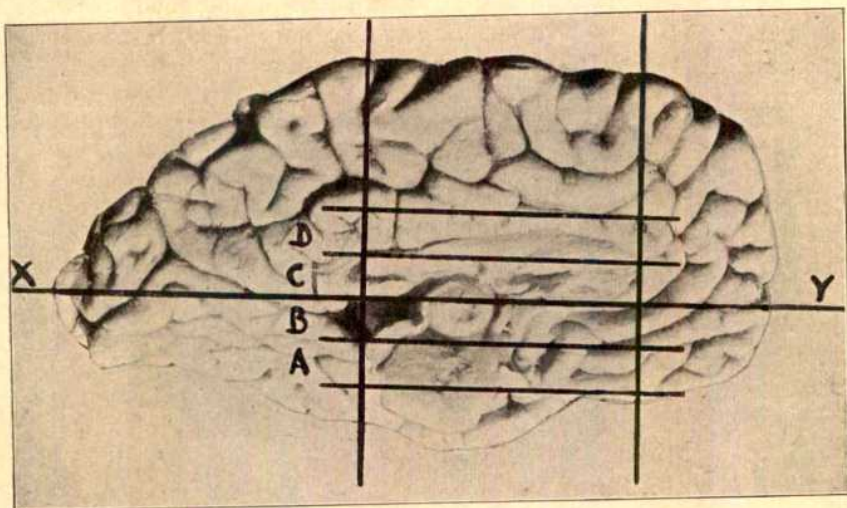


FIG. 38.—Slabs into which the left hemisphere (Case 1) was subdivided for the method of serial sections. Each is 1 cm. thick. x—y as in fig. 37.

(a) *Description of the Appearances of the Lesions on Serial Section.*

(i) *Right side.*—The lesion began, on vertical transverse section, well towards the anterior extremity of the putamen, on a plane which passes through the tips of the temporal lobes, and at a level where the lenticular nucleus is continuous with the caudate round the anterior fibres of the internal capsule. Here a small hole made its appearance almost exactly in the middle of the putamen, and extended by a very narrow process into the internal capsule, the fibres of which it separated but did not appear to destroy. It looked as though the morbid process had extended along one of the "bridges" of grey matter that unite the putamen and the caudate across the capsule.

A few sections further back the cavity was about the size of a split pea, and had a very definitely thickened lining or wall to it, apparently not of recent formation.

At the level of the anterior tip of the globus pallidus (middle lenticular

zone) the lesion was still confined to the putamen. It was rather larger, but remarkably circular. The external capsule stained rather faintly towards its lower part, and was evidently thinned. The external medullary lamina of the lenticular nucleus had disappeared. The pencils of fibres passing mesialwards from the putamen were absent.

Further back, the lesion had spread into the middle zone and destroyed it completely, and had now its greatest diameter in a vertical direction. The

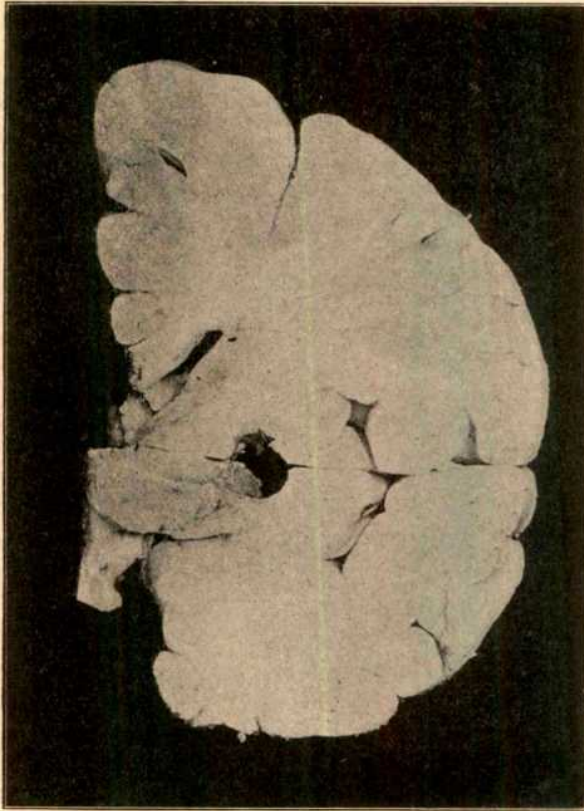


FIG. 39.—Corresponds to line 4—4 of fig. 37. Vertico-transverse section. Cavity in place of lenticular nucleus. Internal capsule intact.

internal medullary lamina could be distinguished, but it was considerably degenerated. The internal capsule was intact, however. The external capsule was somewhat attenuated, and the claustrum was affected, while the fibres of the upper convolutions of the island of Reil also seemed somewhat degenerated. The striothalamic fibres which cross the capsule to the external nucleus of the thalamus were found under a higher magnification to be greatly degenerated, and to be of irregular thickness and staining power; many were

moniliform. On the other hand, some of the bundles of fibres crossing the capsule were normal; probably some at least of these were coming in a reverse direction, from the thalamus. As for the globus pallidus—all that remained of it—its fibres were in a state of profound degeneration; they were twisted,

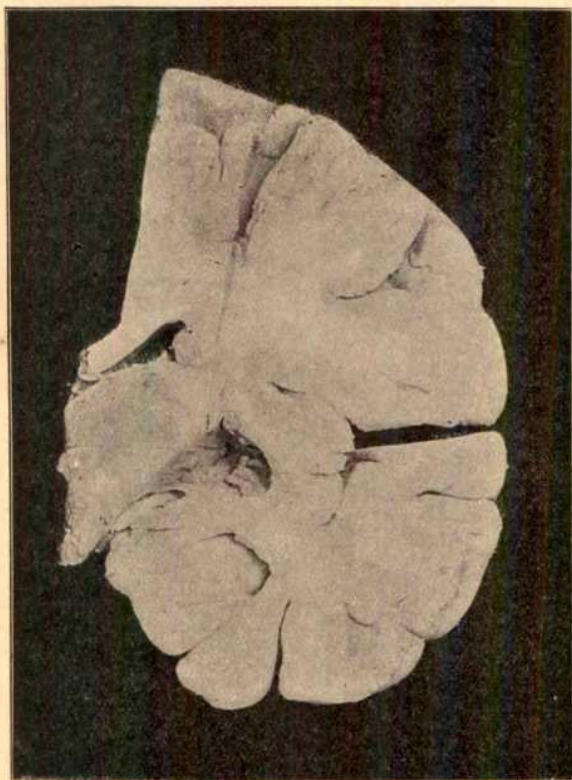


FIG. 40.—Corresponds to line 5—5 of fig. 37. Vertico-transverse section. Posterior end of lenticular cavity is well shown. Note the normal sized optic thalamus.

distorted, wavy, irregular in thickness; some showed a myelin sheath ending in a knot. Many stained badly. They were no longer arranged in close-set symmetrical bundles intersecting each other. The ansa lenticularis was found to consist of a few healthy fibres with many obviously degenerated fibres. All that was left of the putamen proper was a fibreless ring of degenerated tissue round the cavity.

A few sections further back the area of maximum disintegration was reached (fig. 41). The putamen and the middle lenticular zone were non-existent, and their place was taken by an irregular cavity which extended close up the internal capsule on the inner side, and to the claustrum on the outer. The internal lamina of the nucleus could be traced, but it was obviously degene-

rated; the fibres of the internal zone were greatly interfered with, and many of them were in a condition of decay. The internal capsule had some degenerated fibres in it, mostly towards that part of it which forms the genu. In the ansa lenticularis were a great number of defective fibres, along with some that seemed structurally to be normal. It could be traced, staining imperfectly,

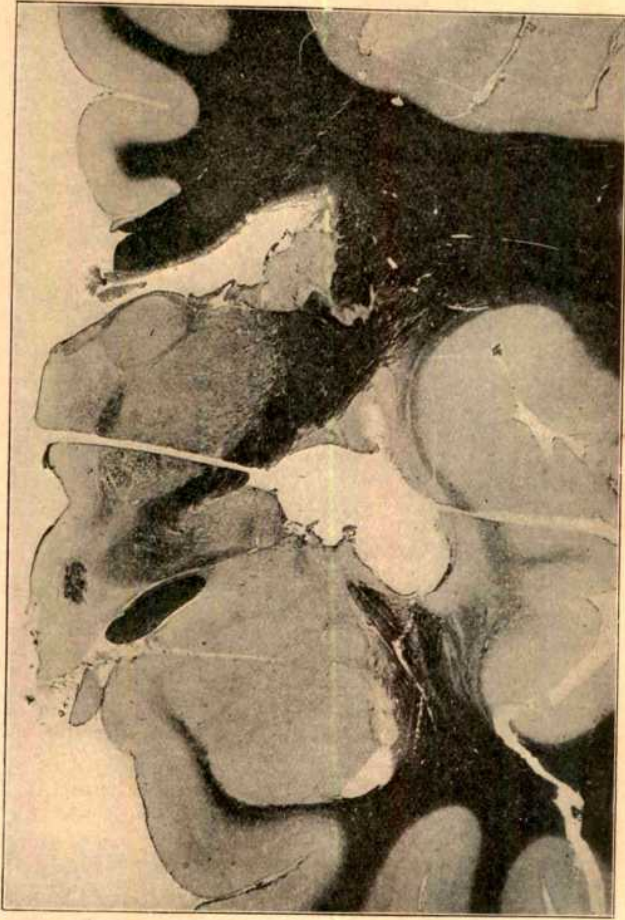


FIG. 41.—Vertico-transverse section No. 148. (Case 1.) Weigert-Pal. (About $\frac{1}{4}$.) See description in text.

round the inner end of the capsule, towards the posterior and inferior part of the thalamus. The striothalamic fibres presented the same features as have already been noted. The external capsule was much thinned through the greater part of its extent. The fibres under the cortex of the upper convolutions of the island of Reil stained feebly ("capsule extrême"). The external medullary lamina of the optic thalamus was poorer in fibres than normally, and

the "zone grillagée" also was much less distinct than in the normal brain. The caudate at this level was somewhat shrunken and contained one or two minute areas of disintegration, and the lenticulo-caudate fibres were grossly degenerated.

The lesion came to an end by gradually narrowing to a point just short of the posterior inferior extremity of the putamen (fig. 42).

Artefact,
owing to
section
being at
bottom of
block.



FIG. 42.—Vertico-transverse section No. 184. (Case 1.) Weigert-Pal. Posterior end of generated lenticular area. Note deeply staining internal capsule, also degeneration in posterior inferior part of thalamus (Forel's bundle, &c.).

A scrutiny of these serial vertico-transverse sections shows that there are certain secondary degenerations which require to be studied.

The ansa lenticularis, considerably degenerated, could be followed into the subthalamie region. Here it became difficult to trace; apparently some of its fibres joined others coming more directly across the capsule to the upper side of the corpus Luysii (strio-Luysian fibres), but its prolongation towards the capsule of the red nucleus could not be made out, presumably because of degeneration.

The corpus Luysii was undoubtedly smaller than normal and somewhat degenerated: under a high power the fine myelinated fibres contained in it were found to be thinned and reduced in number. Some were moniliform.

The lenticular bundle of Forel in the regio subthalamica was also degenerated, but not so much as the ansa, for a number of the fibres passing obliquely across the capsule from the inner zone of the globus pallidus and going to form part of Forel's bundle seemed normal. These were fibres arising from almost the only part of the lenticular nucleus that had escaped destruction. It is possible that some at least of these fibres were of subthalamic origin, passing in the reverse direction.

As regards the optic thalamus, it has been already remarked that the external medullary lamina was poorer in fibres than in the normal brain, irregular, and difficult to trace. The ganglion as a whole was not atrophic, and the fibres that skirt its nuclei were easily traceable. There was diminution of fibres, however, in the neighbourhood of the external nucleus.

The caudate nucleus throughout contained bundles of fine fibres passing down and across the capsule, and the majority of these appeared normal. They were, however, somewhat reduced in number. Towards the posterior part of the caudate rather more of these internuncial fibres were degenerated, including probably all that go from the putamen to the caudate.

The internal capsule stained with normal intensity all through the series of sections, except that it contained a few degenerated fibres in the immediate region of the genu. To all intents and purposes the corticospinal path was perfectly intact.

Türek's bundle was normal.

Retrograde degeneration, or any diffuse degeneration, is so difficult to follow in sections stained by the Weigert-Pal method that nothing can be said of any possible alteration in the corona radiata or in cortical fibres.

(ii) *Left side*.—The condition of affairs on the left side so closely resembled that on the right that a briefer description will suffice.

The lesion extended to the extreme lower and posterior portion of the putamen, behind the anterior commissure, and behind the spot at which the lenticulo-striate vessels enter the hemisphere to run vertically upwards. At a slightly higher level a cavity appeared also in the anterior portion of the same outer zone of the lenticular nucleus, and passing up it is found that where these two cavities united complete destruction of the putamen and of the outer part of the globus pallidus resulted, leaving a fragment of the inner part at its anterior end in which the nerve fibres that remained were all grossly degenerated (fig. 43). Where the lesion was at its maximum, about the middle of the putamen, considered vertically, was that little extension through the fibres of the internal capsule, at its genu, to which allusion has already been made. The little subsidiary cavity thus formed was lined by capsular fibres which stained deeply, but there is no doubt that a number in this section of the capsule were degenerated, for the degeneration could be traced. It was not, however, as pronounced as might have been expected from the

naked-eye appearance. There were also two very small holes in the outer part of the optic thalamus, close up to the capsule, as well as the other small punched-out depression which is seen in fig. 44. The lesion extended almost to the upper limit of the putamen, coming gradually to an end. A minute prolongation into the capsule, or rather through it, could be seen at the upper termination of the lesion.

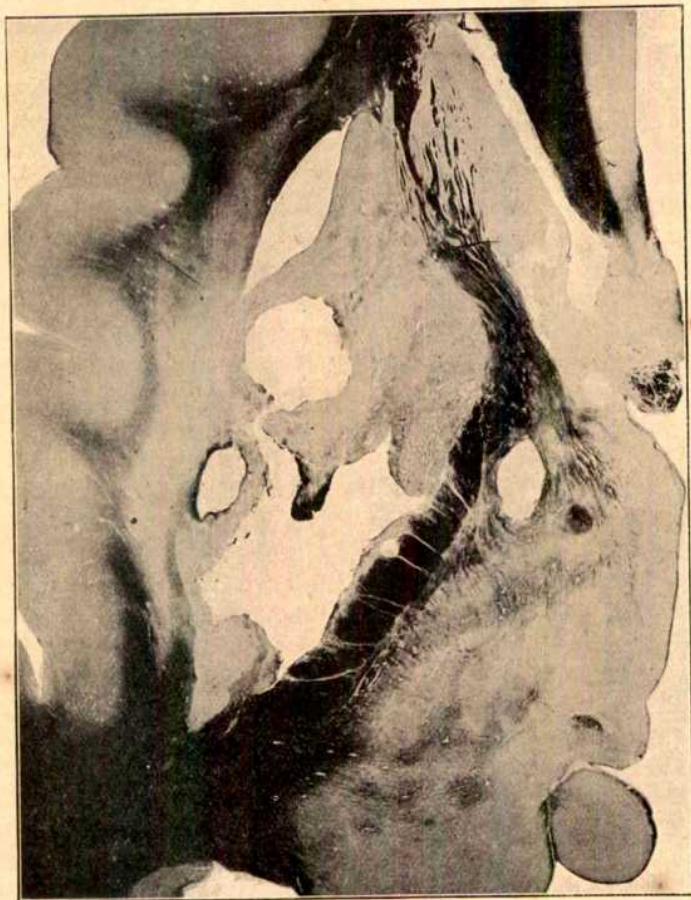


FIG. 43.—Horizontal section No. B 31, left hemisphere. (Case 1.) Weigert. (About $\frac{7}{8}$.) For description see text.

It is noteworthy that the external capsule was degenerated only towards the site of the maximum area of disease, for it was quite normal above, although the putamen was still completely softened. The convolutions of the island of Reil were more affected, i.e., their fibres stained less well towards the lower part of the island, but they did not appear to be softened or to have lost any substance. The claustrum was invaded apparently only in one place.

The internal capsule stained with normal intensity throughout, except that as the fibres converged to form the crus, in the subthalamic region, it could be seen that the genu bundle was partly degenerated. This degeneration, however, was not extensive. It has been already referred to. The caudate nucleus and optic thalamus were in much the same condition as on the opposite side. The optic thalamus was not directly affected at all, except for one or two very minute punched-out little cavities; it is noteworthy that no thalamic symptoms were present during life. In the horizontal sections the corpus Luysii was seen

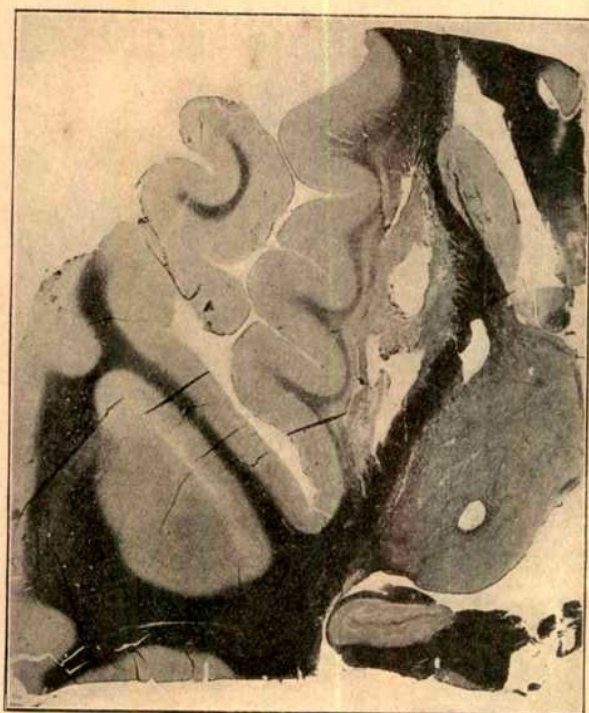


FIG. 44.—Horizontal section No. C 39. (Case 1.) Weigert. For description see text.

to be shrunken, and smaller than normal; the ansa lenticularis was degenerated, the lenticular bundle of Forel, and the strio-Luysian fibres which cross the pyramidal tract more or less obliquely, were partly degenerated, especially the former; amongst the latter there were a number of normal fibres; the red nucleus did not appear either to be smaller or to contain fewer fibres than in the normal brain. It is difficult to say whether the locus niger showed any pathological change; apparently not. As on the right side, the strio-thalamic fibres were much degenerated; the external medullary lamina of the thalamus was less marked than it should be; the "zone grillagée" of

Dejerine was scarcely distinguishable; the fibres in the neighbourhood of the external nucleus were considerably reduced in number.

In the Weigert-Pal sections, towards the base of the left hemisphere the shrinkage and cavitation of the outer lenticular segments, coupled with the gross degeneration of the densely packed fine fibres of the inner segment, and the secondary degenerations above referred to, the poor staining of the fibres of the convolutions of the island of Reil, the involvement of the external capsule—were all well seen.

(b) Minute Anatomy of the Degenerated Area.

Under a low power the walls of the cavity were seen to be composed of a thick interlacing network of neuroglial fibres, with neuroglia cells, degenerated myelinated fibres, diseased and fragmented blood-vessels and capillaries, all

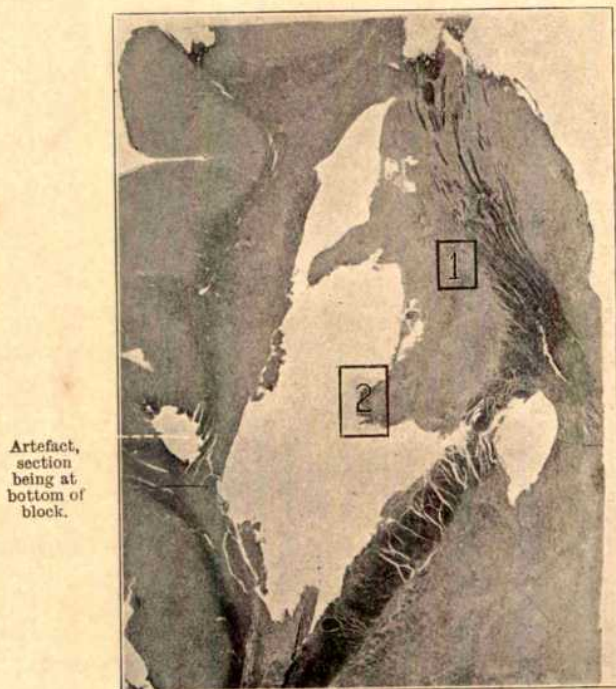


FIG. 45.—Photograph of maximum degenerated area (section imperfectly stained) to show situation of figs. 46 and 47 (1 = 47; 2 = 46).

mixed up inextricably. Along the margins of the cavity it was common to come upon such blood-vessels as are represented in fig. 46. It is noteworthy that while they were reduced to mere débris, none of them was

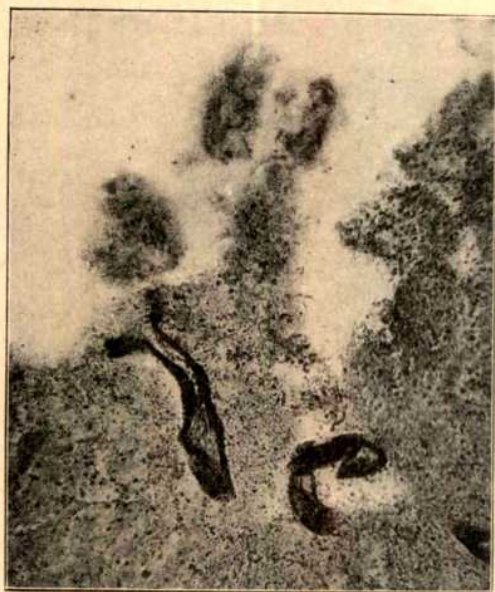


FIG. 46.—Margin of lenticular cavity. ($\times 60$.) Haematoxylin-Van Gieson. (Corresponds to [2] of fig. 45.)



FIG. 47.—Degenerated fibres in globus pallidus. Weigert-Pal. (Corresponds to [1] of fig. 45.)

thrombosed or occluded. Not a single vessel in this condition was found in more than a score of sections. In some places the cavity wall was clean cut, firm, and evidently of old formation; in other places it appeared to be crumbling away. In the fragment of the globus pallidus that remained one or two nerve-cells could still be found, atrophic and staining deeply. Here the confusion of degenerated medullated nerve-fibres was at its maximum. (See fig. 47.)

In the small areas of putamen and globus pallidus that had not entirely succumbed the condition of the blood-vessels was investigated. One or two seemed to have undergone a sort of hyaline change, their coats staining in a homogeneous way, and being rather difficult to differentiate. In others the

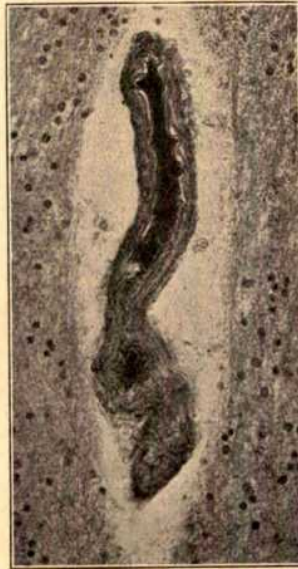


FIG. 48.—Artery from globus pallidus. Hæmatoxylin-Van Gieson. Normal walls. (It has a plug of bacilli in its lumen.)

muscular and adventitial coats seemed thickened in proportion to the intima, which in no instance showed any sign of endarteritis. Many vessels were quite normal (fig. 48). No indication of small-cell infiltration was to be found round the vessels, in the lymphatic sheaths, or where the lenticular nucleus was degenerated. It is probable that some, if not most, of these changes in the vessels were of a regressive nature, and not the cause of the degeneration of the nucleus, but the result (fig. 49).

The sections of the middle cerebral artery and its branches, treated separately, showed no recognizable pathological change.

Under a higher magnification "Körnchenzellen" could be seen in the part of the globus pallidus that was left, but they were not present in numbers.

(8) *Cortex cerebri*.—The cortex cerebri was investigated by Nissl's method, as well as with hæmatoxylin-Van Gieson. Pieces were taken from various parts of the motor area on both sides, as well as from frontal, occipital, and temporal lobes.

In the precentral gyrus, certain changes were found, more obvious in some sections than in others. While the great majority of the Betz-cells were



FIG. 49.—Degenerated blood-vessel from near margin of lenticular cavity. (Case 1.) Hæmatoxylin-Van Gieson. Thickening of middle and outer coats. Lumen patent. No small-cell infiltration. The changes are probably secondary to the lenticular degeneration.

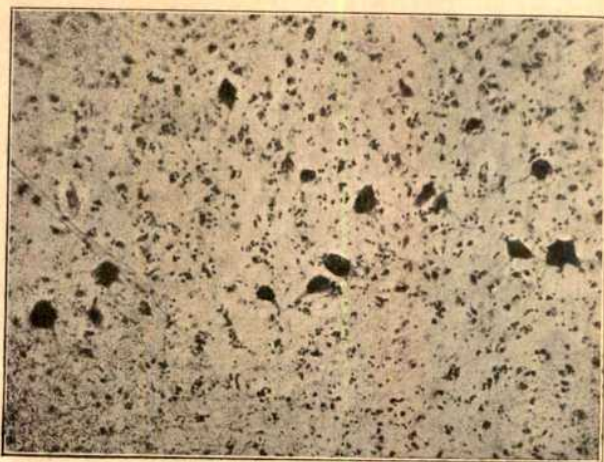


FIG. 50.—Oblique section from right leg centre, paracentral lobule (Case 1). Nissl. Normal Betz-cells.

normal, a few showed pigmentary degeneration, with some tigrolysis, presumably a change of a fairly chronic regressive type. Their numbers were not diminished to any extent. In the shoulder area the Betz-cells were practically all normal. In sections from the leg centres the appearances were more or less normal. Thus in fig. 50 (right leg centre) it can be seen that

the Betz-cells are of normal size, shape, and staining properties. The same was the case with the left leg centres. The other layers of the cortex in the precentral gyrus could be readily distinguished and did not seem deficient in any way.

In view of the almost complete helplessness of the patient, and in view of the spasticity, tremors, and contractures, the practically normal condition of the cyto-architectonic structure of the motor area, and the integrity of the corticospinal tracts, are facts of great importance.

The cortex of other parts of the brain showed changes so slight that it is difficult to know what importance to attach to them. Occasional pigmentary degeneration of pyramidal cells occurred, but there was no wholesale disappearance of cells, or confusion of cell layers. The cortex was of good depth everywhere.

In no one of many scores of sections examined was there any trace of small-cell infiltration of cortical vessels, so that the pathological picture was very different from that of dementia paralytica.

In sections of the motor cortex stained by Pal's method for myelinated fibres, it was seen that the tangential layer of fine fibres was considerably reduced, but the supraradiary and intraradiary networks were not altered to any extent.

MICROSCOPICAL EXAMINATION OF OTHER ORGANS.

(1) *Liver*.—The histological methods utilized were hæmatoxylin-eosin, hæmatoxylin-Van Gieson, carbol gentian violet, Weigert's stain for elastic tissue, Sudan III for fat.

Under a low magnification the appearance represented in fig. 49 was met with. Numerous islets of liver-tissue, not a few of which did not contain more than one or two liver units, while others were much larger, were separated from each other by wide strands of cirrhotic tissue, which in some places was mainly fibrous, in others very cellular. Occasionally a few isolated liver-cells, as was determined by the method of serial sections, were noted to be surrounded by cirrhotic strands. There was little indication, however, of any intralobular spread of connective tissue, so that the monocellular type of cirrhosis was not in evidence. In the more cellular areas of cirrhosis abundant bile-ducts ramified in all directions.

The condition of the liver-cells was highly irregular. Many lobules appeared to be normal, the columns of cells being symmetrically radiate, staining well and of good size. In other nodules scarcely a single normal cell was found; many were in a necrotic state, shrunken and staining homogeneously a brighter tint with eosin than normal cells. Everywhere there were evidences of fatty degeneration. On the other hand, more particularly towards the periphery of some of the nodules, regeneration of liver-tissue was actively proceeding. Thus it was common to find the nuclei of the cells enlarged; some were dumb-bell-shaped and evidently about to divide by

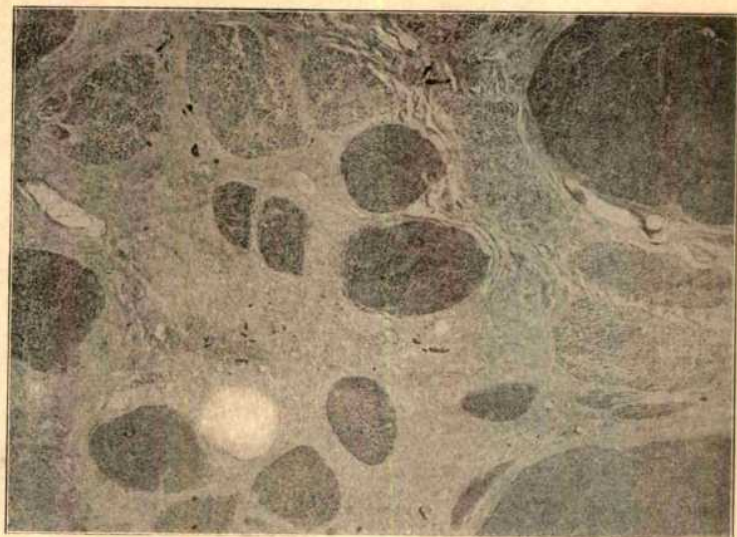


FIG. 51.—Liver (Case 1). Hematoxylin-Van Gieson. Irregular size of liver-nodules. ($\times 20$.)



FIG. 52.—Liver-cell dividing by an amitotic process. Hematoxylin eosin. ($\times 1,000$.)

an amitotic process (fig. 52). Other cells were doubly nucleated. In the regenerating areas metachromatic staining of the nuclei was common. No definite mitotic figures were seen; apparently this form of multiplication is much less frequent than the other.

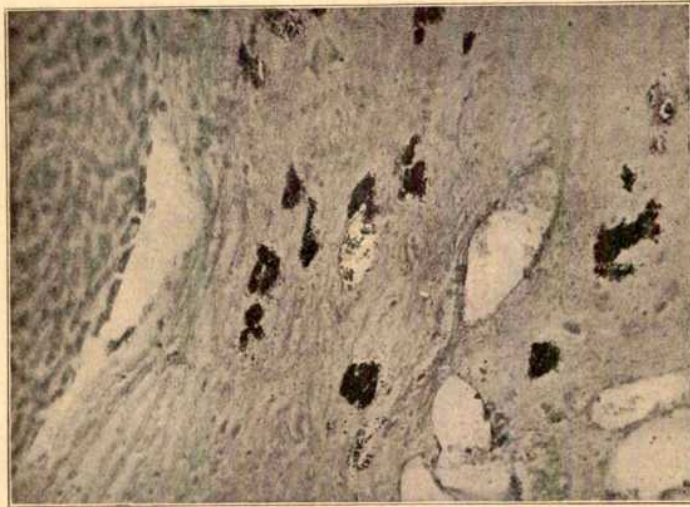


FIG. 53.—Clumps of bacilli in cirrhotic liver-tissue (Case 1). Carbol gentian violet. ($\times 60$.)



FIG. 54.—Bacilli in neighbourhood of portal tract (Case 1). Carbol gentian violet. ($\times 750$.)

The portal tracts and vessels of the organ did not show any particular alteration beyond an increase in connective tissue round the tracts. There was no indication of inflammatory processes, in particular, no small-cell

infiltration. A few plugs of inspissated bile were found. There was no sign of any obliteration of bile-ducts.

(2) The *suprarenals* did not present any obvious morbid change.

(3) The *thyroid* showed certain regressive changes in the shape of interstitial overgrowth and diminution of colloid.

There remains to be described only one other pathological condition, but this is a widespread one. In every organ examined, particularly in the liver, in the gall-bladder walls, and in the central nervous system, bacterial invasion was acute. Clumps of short bacilli, structurally rather like the *Bacillus coli communis*, were seen everywhere in sections of the liver, and were found plugging the vessels of the degenerated lenticular area (see fig. 48), in the cortex cerebri and cerebelli, and in the spinal cord. The appearances presented in the liver are reproduced in figs. 53 and 54. The widespread nature of the condition suggests a terminal infection, which, it is known, can take place with extraordinary rapidity. It is probable that the infection was from the alimentary canal, as the patient had neither bed-sores nor cystitis. It is difficult to believe that the infection is of any special pathogenic significance.

RÉSUMÉ OF THE PATHOLOGICAL FINDINGS IN CASE 1.

The brain is of good size, shape, and weight. The cerebral gyri are not atrophic, are of normal convolitional pattern, and present no obvious morbid appearance. The membranes are to all intents and purposes normal. The cerebral blood-vessels are not thickened or occluded, and show no patches of disease in their walls.

On Marie's *coupe d'élection*, the eye is at once caught by a complete bilateral and symmetrical destruction of the lenticular nucleus. In place of the latter, on either side, and more especially in place of its outer and middle zones, is an elongated cavity, measuring $2\frac{1}{2}$ cm. long by $1\frac{1}{4}$ cm. wide, with dark-coloured crumbling walls, extending from the anterior to the posterior limit of the putamen, and from its extreme lower extremity almost to its upper limit. Only a small piece of the inner zone of the globus pallidus remains. Compared with this utter degeneration of the lenticular nucleus, the optic thalamus and the caudate nucleus are well preserved, except that in the former, on the left side, there is a small punched-out hole towards its posterior part, and the latter is on both sides a little shrunken, and less full and rounded than in a normal brain. The degenerated area extends close up to the internal capsule on both sides; on the right this seems quite intact throughout, although it is found to be somewhat undermined; on the left there is a small prolongation of the cavity across the genu of the capsule, the fibres of which are separated rather than destroyed.

Microscopically, however, there is some descending degeneration in the genu fibres.

The external capsule is thinned on both sides, and degenerated in its middle third; the claustrum is very slightly invaded on the left side; the cortex of the island of Reil is well preserved on both sides, although microscopically there is some degeneration of the subcortical fibres of its convolutions towards its posterior part.

The white matter of the cerebral hemispheres is normal. The cortex is practically normal; in particular the origin of the pyramidal tracts in the Betz-cells of the motor area is carefully examined, and the great majority of the latter are found to present no morbid appearance, although some show chronic degenerative changes.

With the exception of the slight descending degeneration in some capsular genu fibres on the left side, the pyramidal tracts stain normally throughout, and, followed from the motor cortex through the capsule, crus, pons, medulla and cord, are perfectly normal.

On the other hand, the extrapyramidal system from the lenticular nucleus, via the ansa lenticularis, to the red nucleus, is degenerated on both sides; the lenticular bundle of Forel is partly degenerated, as are a large number of the strio-Luysian fibres on both sides; the corpus Luysii is smaller than normal. The cells of the red nucleus do not appear changed, nor does the nucleus seem altered in its fibre-content. The striothalamic fibres are degenerated.

The external medullary lamina of the optic thalamus, the "zone grillagée," and the outer part of the thalamus generally, are to a certain extent altered.

The pons and medulla, and the cerebellum, are not the seat of any change that can be recognized microscopically.

The nuclei of the cranial nerves are unchanged, except for slight alterations of secondary significance.

The spinal cord (cells and fibres) is normal, except for certain slight alterations, also of secondary significance.

The same is true of the muscles.

The liver is in an advanced state of cirrhosis; the type is mainly multilobular, but some monolobular cirrhosis is found. In the cirrhotic tissue abundant bile-ducts ramify. The liver-cells are in many instances normal, others are necrosed, many show fatty infiltration and degeneration, others are actively regenerating.

The spleen is not enlarged. The thyroid shows interstitial changes.

There are evidences in all the organs examined, particularly in the liver and nervous system, of a terminal bacterial infection.

Case 2.—The autopsy was performed by Dr. W. H. B. Stoddart and myself on March 4, 1907, thirteen hours after the death of the patient.

The body was greatly emaciated, but there were no bruises or bed-sores. The skullcap and the dura mater with its veins and sinuses presented no abnormality. The cerebral arteries at the base of the brain were all normal, patent, and showed no visible thickening or patchy degeneration. There was

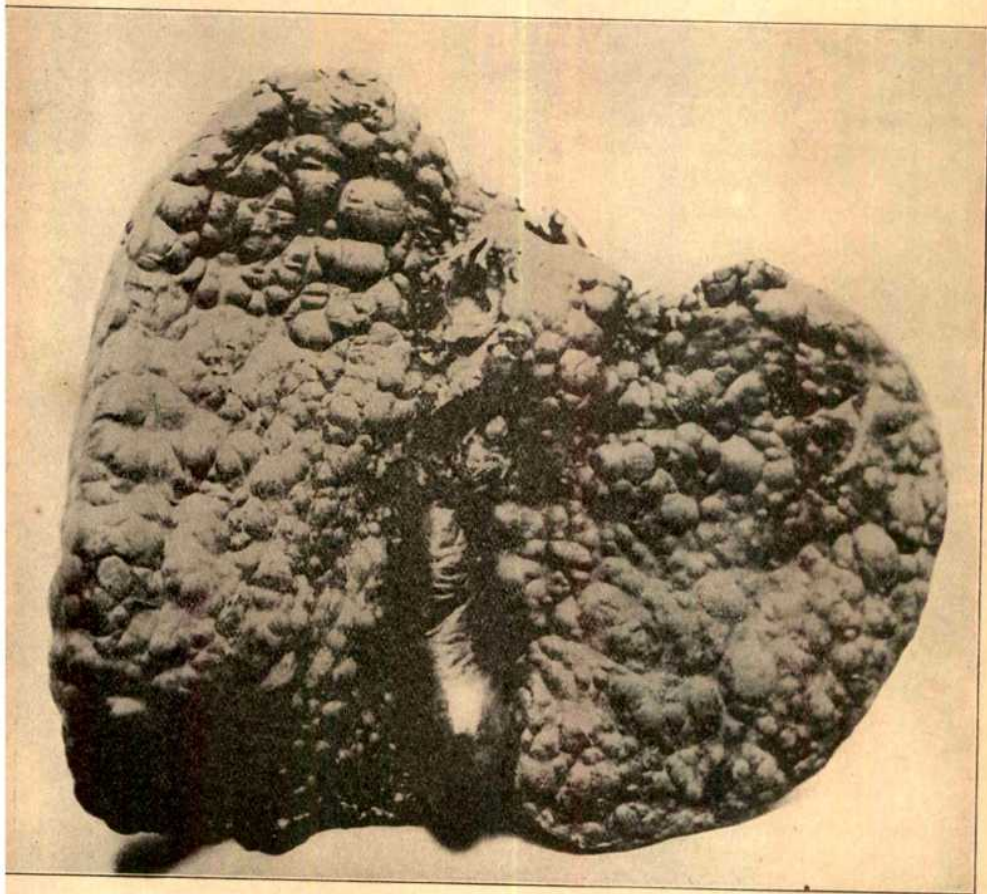


FIG. 55.—Liver, under surface (D. P., Case 2).

excess of cerebrospinal fluid on opening the membranes, especially in the subarachnoid spaces. The brain looked œdematous, and the convolutions somewhat separated from each other. It weighed 1,275 gm. The pia-arachnoid appeared slightly thickened in one or two areas.

The bronchial vessels were congested, and there were several patches of pneumonic consolidation scattered throughout both lungs, the largest patch being at the apex of the lowest lobe of the right lung. The heart was normal.

The spleen was enlarged, and weighed 312 gm., but it showed no obvious morbid appearance on section. The kidneys were normal.

The liver presented a remarkable appearance. It was in an advanced state of multilobular cirrhosis, being subdivided up into spherical portions of liver substance about the size of small hazel-nuts, held together by bands of cirrhotic tissue. It was firm, and tended to preserve its shape. Its weight was 1,392 gm.

Figs. 55 and 56 show the naked-eye appearances of that organ. One of

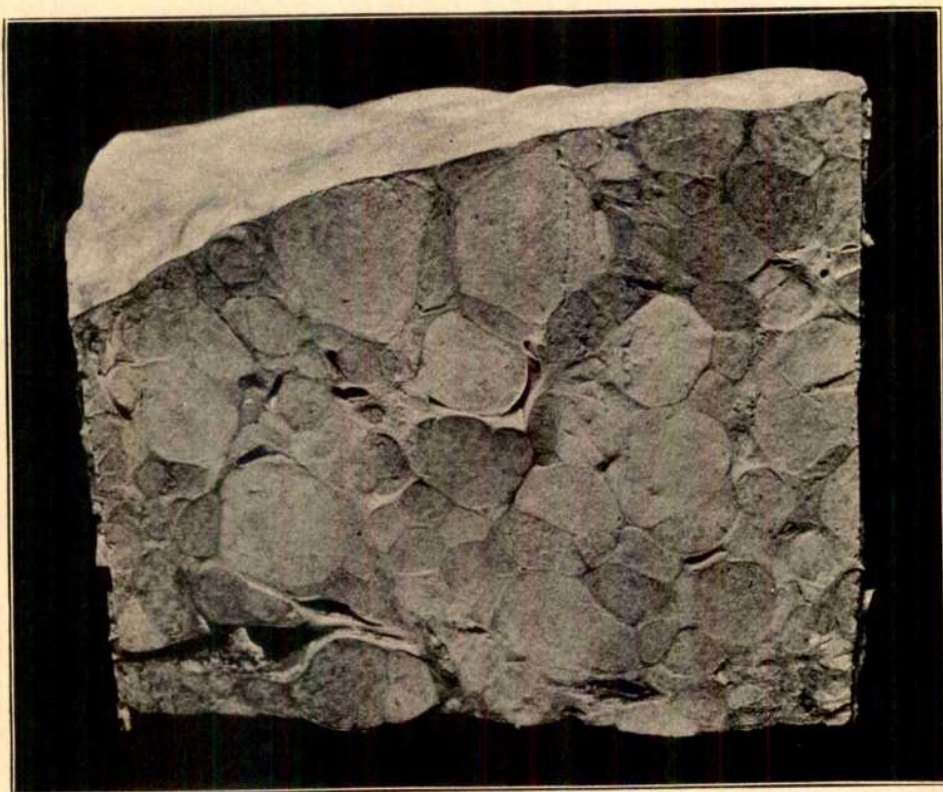


FIG. 56.—Liver, transverse section (D. P., Case 2). Natural size. The general character of the cirrhosis and the varying appearance of the nodules are well shown.

them (fig. 56) was taken after the liver had been in formalin for about twelve months, and it shows the appearance on transverse section. The irregular size of the nodules and the difference in their colour are well brought out. Some were much darker than others, while many looked somewhat mottled. The strands of cirrhotic tissue were notably slender in comparison to the dimensions of the nodules which they enclosed. There was some thickening along the portal tracts. The capsule of the organ was slightly thickened.

When it was removed from the body it was not noted to be bile-stained; the gall-bladder was in a normal condition.

* MACROSCOPICAL EXAMINATION OF THE CENTRAL NERVOUS SYSTEM.

Owing to an unfortunate accident the nervous organs were rendered almost useless for certain methods of investigation, so that to some extent it must be considered incomplete. What I am able to describe, however, will be sufficient to class the case *in toto* with No. 1 and No. 3.

The brain, when stripped of its membranes (which were not adherent) was found to be of good size, shape, and convolutional pattern. On a transverse horizontal section through the right hemisphere, the putamen was found to be darker in colour than usual; it was shrunken and soft. There was not, however, any gross loss of substance—i.e., no cavitation. The globus pallidus also appeared somewhat shrunken, while the optic thalamus, the caudate nucleus, and the internal capsule were normal. I am unable to say what the condition on the left side of the brain was, and whether there was any similar degeneration of the outer zone of the lenticular nucleus. On the right side the internuncial fibres from the outer to the middle zone of the nucleus were almost entirely absent, and the outer lamina was not readily distinguishable. The fine fibres of the caudate, however, could be seen easily. The external capsule and the white and grey matter of the convolutions of the island of Reil presented no obvious morbid appearance.

No other change was demonstrable on this section by Marie's *coupe d'élection*. The cerebral cortex appeared to be of good depth everywhere, with the possible exception of the first and second frontal convolutions, where it may have been a little thinned. The white substance of the hemisphere presented no abnormality. There was no hydrocephalus, and no ependymitis.

The pons, medulla and cord, and the cerebellum, looked quite normal.

MICROSCOPICAL EXAMINATION OF THE NERVOUS SYSTEM.

(1) The *muscles* and the *peripheral nerves* were not examined.

(2) *Spinal cord*.—The methods of staining employed were Weigert-Pal, Nissl, and hæmatoxylin-Van Gieson.

The meninges were everywhere normal. There was no trace of pachy- or lepto-meningitis: in particular, there was no small round-cell infiltration of any sort. The spinal vessels, both intra- and extra-medullary, were normal, and showed no sign of endarteritis.

The spinal cord, from the point of view of its myelinated fibres, was normal. In particular, there was no trace of any degeneration in the pyramidal tracts. The medullated fibres of the grey matter of the cord were likewise normal, if perhaps a little sparser.

Examined by Nissl's method, the cells of the anterior horns were found to be present in good numbers, to stain well, and to preserve a normal size and

shape in the great majority of them. Some were slightly shrunken and elongated, staining unusually deeply, but remaining nucleated. Others were in a state of commencing pigmentary degeneration, but there were not any, as far as was noted, that showed an acute form of degeneration associated with excentricity of the nucleus and pulverization of the tigroid substance round it.

(3) *Medulla, pons, and cerebellum.*—The same methods were employed for the examination of these structures as for the cord.

With the Weigert-Pal stain no defect was to be seen in the corticospinal tracts anywhere. They stained deeply, and were not degenerated in any way. The transverse sections of the medulla (fig. 57) and pons that were examined seemed normal in all respects. Similarly with the cerebellum, its nuclei and peduncles did not show any deviation from the normal.

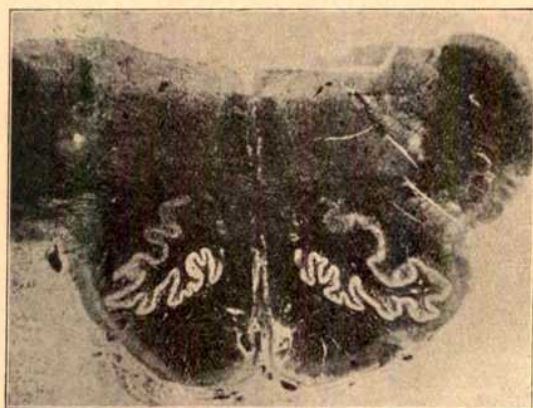


FIG. 57.—Medulla (Case 2). Weigert-Pal. (The marginal ring of "bleaching" is due to the piece having been accidentally left in absolute alcohol.)

The nuclei of the cranial nerves, especially the facial and the hypoglossal, showed no pathological change by Nissl's method. The cells were present in good numbers, with normal staining reactions.

(4) *Crus cerebri.*—The pyramidal path in the crus was unimpaired. The red nucleus was not altered in its fibre-content, nor in its cells, as seen when stained with hæmatoxylin-Van Gieson.

(5) *Basal ganglia and internal capsule.*—The appended description applies to the right side only, and is of necessity somewhat incomplete. The histological methods utilized were the same as for the cord.

In the degenerated right putamen there was considerable overgrowth of neuroglial tissue, forming a fairly thick feltwork; it was in some places sparse and evidently breaking down. Great numbers of glial nuclei were to be seen. In the degenerated area there were no signs of inflammatory reaction.

The important feature of sections through the lenticular nucleus was the dearth of nerve-cells, both in the putamen and the globus pallidus, but particularly in the former, which was almost cell-less. The blood-vessels were neither thickened nor obliterated, but stood out prominently, usually with enlargement of the Virchow-Robin space, and were often apparently somewhat dilated, possibly a little thinned (fig. 58). There was no trace of

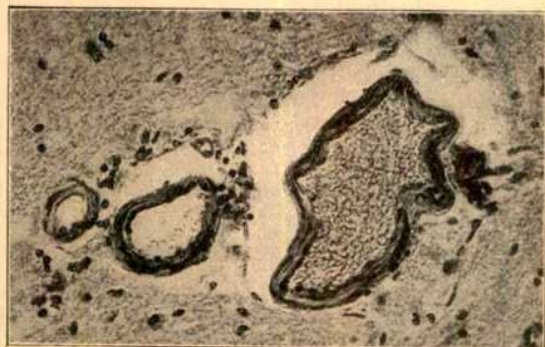


FIG. 58.—Vessels from the right putamen (Case 2). Hematoxylin-Van Gieson. Normal walls. No small-cell infiltration.

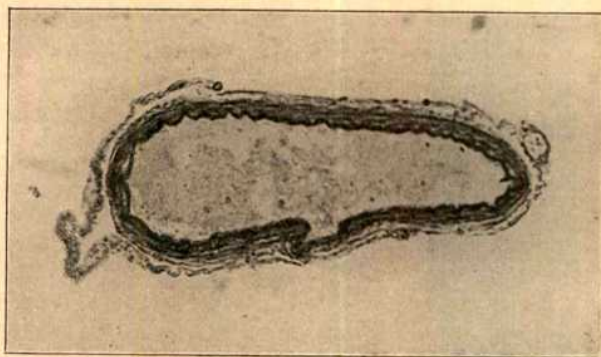


FIG. 59.—Transverse section of a lenticulo-striate artery, removed from degenerated area and cut separately (Case 2). Hematoxylin-Van Gieson. The vessel is, if anything, thinned. No trace of endarteritis. ($\times 150$.)

endarteritis; the intima was unaltered. Nor was there any thickening of any of the other coats. Fig. 59 represents a transverse section of one of the lenticulo-striate arteries, removed from the degenerated area and cut separately. Endarteritis was conspicuously absent.

The caudate nucleus showed a slighter degree of the change that was found in the putamen; there seemed to be an increase of glial nuclei, and fewer

nerve-cells than in the normal nucleus. But the changes were slight. From the point of view of cells and fibres, the optic thalamus was practically normal.

The internal capsule throughout stained in normal fashion, and was neither atrophied nor hypertrophied. Both its anterior and its posterior limbs were intact. The fibres that cross the internal capsule, running between the globus pallidus and the optic thalamus (striothalamic), were mostly normal. They stained well, and were not diminished in numbers. Some, however, were degenerated. The inner lamina, between the middle and inner zones of the lenticular nucleus, was well developed, but the fibres that pass mesially from the putamen to the globus pallidus were greatly diminished in number, and to a great extent degenerated, except at its anterior and posterior extremities. The external capsule did not seem to be involved in the disease, and the fibres of the white matter under the convolutions of the island of Reil were normal, except in one place, opposite the centre of the putamen, where they did not stain well with Weigert-Pal.

In this case, unfortunately, it was impossible to examine further the lower portions of the degenerated area, so that the condition of the ansa lenticularis is not known, nor of the structures in the subthalamic region.

(6) *Cortex cerebri*.—Pieces were taken from both sides of the brain, including in particular the motor area, with both the precentral and the postcentral convolutions.

It may be said at once that from the cyto-architectonic point of view no definite changes could be made out. The Betz-cells of the motor area were easily recognizable, present in quantity, and not altered in staining reactions or in morphological characters, except that a few showed commencing pigmentary degeneration. The cells of the pyramidal layers did not appear to be altered, though round many of them parasite neuroglial cells were to be seen. The depth of the motor cortex was not appreciably different from the normal brain.

The cortex in the other areas examined did not show any pathological change that need be specified.

From the myelo-architectonic point of view only the fibre-content of the motor area was investigated, and it proved to be normal, with the exception of considerable diminution in the tangential layer, and to a less extent of the supraradiary network.

Nowhere in the cortex were the vessels surrounded by small-cell infiltration, nor was there any sign of increased neuroglial growth.

MICROSCOPICAL EXAMINATION OF OTHER ORGANS.

The only other organ subjected to examination was the liver, which was stained with hæmatoxylin-eosin, hæmatoxylin-Van Gieson, Weigert's elastic tissue stain, and Sudan III.

Under a low power the liver-nodules presented a varied appearance. Some

contained one or two lobules only; the majority contained as many as eight or twelve; some were evidently in full functioning power, as the columns of liver-cells were normal; others were totally degenerated and changed into a mass of fat-granules. In many places in the cirrhotic tissue immense numbers of small connective tissue cells, and great numbers of so-called new bile-ducts, were to be seen. The cirrhotic tissue was slender and nowhere looked very fibrous. In some places there were delicate strands of connective tissue passing between groups of liver-cells. The cells themselves, under a higher magnification, were found in most lobules to stain normally, but in areas where active regeneration was taking place—and of this there was abundant evidence—metachromatic staining was noticed. Regeneration was shown by the presence of enlarged or doubled nuclei; sometimes amitotic division was seen, but no mitotic figures.

There was no special feature to be noticed in the sections stained by Weigert's elastic tissue stain. The picture given with the Sudan III sections was very striking, and explains the irregular coloration showed in the naked-eye photograph reproduced as fig. 56.

RÉSUMÉ OF THE PATHOLOGICAL FINDINGS IN CASE 2.

The brain is of good size and shape, and its convolutional pattern is normal. There is no indication of atrophy of the gyri, except that possibly the cortex of the frontal convolutions is a little thinned. This, however, if present, is so slight as to be negligible. The white matter of the hemispheres shows no abnormality. The membranes are normal, except that in one or two places the pia-arachnoid is a little thickened. The cerebral blood-vessels present no deviation from a normal state. The pons, medulla, and cord look normal.

On section the right lenticular nucleus is seen to be in a definite state of degeneration; it is atrophic in its outer zone or putamen, shrunken, discoloured, looks friable, and feels soft. There is not, however, any gross cavitation. The globus pallidus does not appear to be impaired beyond being perhaps a little smaller than usual; the external capsule is normal. The degeneration in the putamen occupies its whole breadth, but leaves a small portion anteriorly and posteriorly which seems intact. Microscopically there is marked neuroglial sclerosis, overgrowth of glial nuclei and fibres, almost complete disappearance of nerve-cells from the putamen, and considerable involvement of the internuncial fibres from the outer to the inner zones of the lenticular nucleus.

The arteries of the affected area do not show any change, except that they are, if anything, dilated and thinned, in some instances at

least. There is no endarteritis of any vessel, and no small-cell infiltration.

The internal capsule, the optic thalamus and caudate nucleus are normal throughout, except for slight commencing changes in the last of these.

The motor cortex is normal, and the pyramidal tracts, examined from the Betz-cells of the cortex to the anterior horn-cells of the spinal cord, are likewise normal. There is no degeneration in the cord, by any method.

The liver is profoundly cirrhotic, though the bands of cirrhosis are relatively slender; many nodules are reduced to masses of fat, but others are actively regenerating. Numerous bile-ducts course in the cirrhotic tissue.

Case 3.—The autopsy was performed by myself at 7.30 p.m. on the evening of September 21, 1910, twenty-seven hours after death. As the body had been kept in the open air, the sanatorium being at a considerable altitude and the nights very cold, it was in an excellent state of preservation.

Post-mortem lividity was marked. The limbs remained very rigid. There were fairly large superficial abrasions over the heels, trochanters, and sacrum. The body was profoundly emaciated, being reduced almost to skin and bone. The outlines of the muscles, wasted as they were, were unusually distinct beneath the skin. On opening the calvarium the dura was not adherent, nor was it obviously thickened or discoloured. On its being cut open the sub-arachnoid spaces and cisterns were found to be greatly distended with fluid. As a result the brain looked œdematous and the outlines of the convolutions were indistinct through the distended membranes. Over one minute spot at the upper end of the left Rolandic area the dura was adherent to the tissues underneath. The cerebral veins were greatly distended everywhere. Over the base of the brain the arachnoid appeared somewhat thickened, and a little opaque, especially across the pons and the interpeduncular space. Elsewhere that membrane seemed normal, with the possible exception of the portion that covered the anterior parts of the temporal lobes, which also appeared rather opaque. As the brain was being taken out my impression was that the pons was rather small in proportion, and that the cranial nerves were rather slender.

The brain and cord were at once immersed in a 10 per cent. solution of formalin.

The pituitary gland, thymus, left lobe of thyroid, left suprarenal body and left kidney were removed for subsequent examination. The thyroid appeared to be of normal size, and the other organs mentioned above presented no obvious alteration to the naked eye. The spleen was slightly enlarged, felt firm, and on section showed no deviation from the normal, except that it was congested.

The heart and lungs were normal, except that the latter were somewhat

congested. There were a few ounces of clear fluid in each pleural cavity, but no adhesions.

The liver presented a striking appearance, which is seen in figs. 60 and 61. It was of medium size, of good shape, and weighed 1,450 gm. It was firm and preserved its shape well when removed from the body. When examined it was at once seen to be in a state of profound cirrhosis; the dome-like upper surface and the under surface were not smooth, but subdivided up into innumerable small raised nodules, between which were narrow lines where



FIG. 60.—Liver (E. P., Case 3). Under surface.

the surface was depressed, corresponding to bands of cirrhotic tissue. The average size of the nodules was perhaps that of a threepenny-piece, but they varied considerably. In some places they were more evident and more closely set than in others. There were no signs of hepatitis; the capsule was not definitely thickened anywhere, and there were no adhesions to the surrounding viscera. The organ was, if anything, rather lighter in colour than usual; it was not bile-stained, nor was the coloration patchy or irregular. Its appearance on transverse section was equally striking. From one side to the other it was subdivided into more or less circular or oval nodules, or islets, most

of which were about the same size, and were separated from each other by narrow cirrhotic strands. In one or two places the cirrhosis approximated to the monolobular type, but it was far more characteristically multilobular.

There was no ascites.

The following muscles were taken for subsequent microscopical examination: muscles of the left thenar eminence, left flexor sublimis digitorum, right flexor carpi ulnaris, right biceps, right supinator longus.

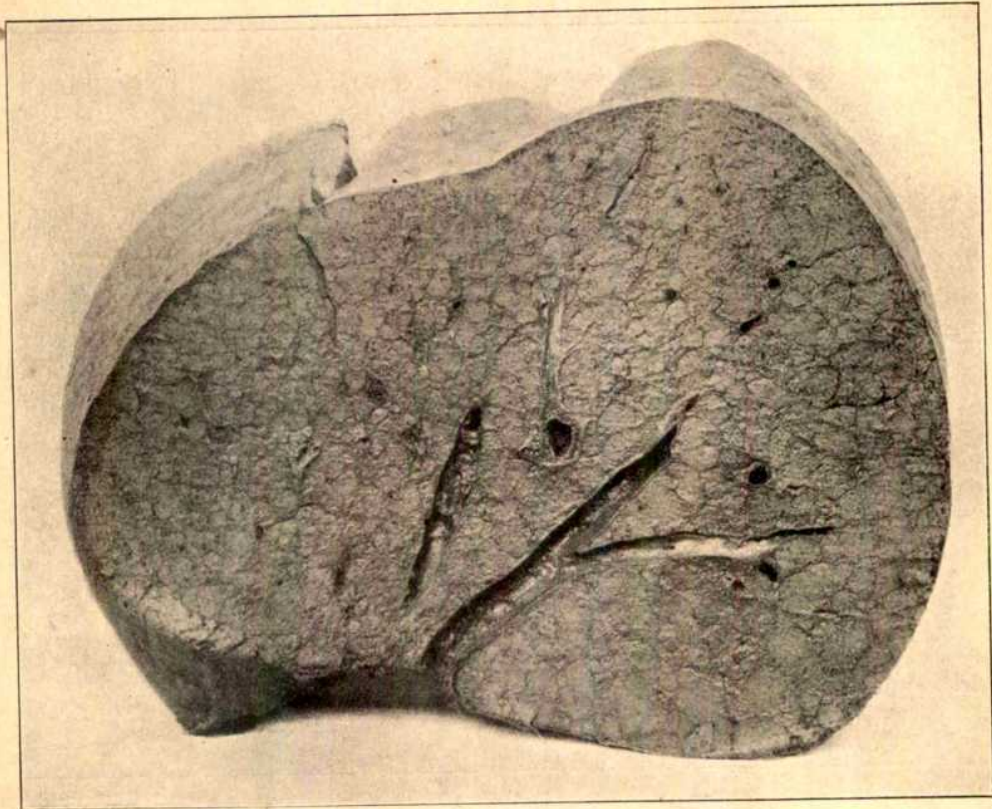


FIG. 61.—Liver, transverse section (E. P., Case 3).

MACROSCOPICAL EXAMINATION OF THE BRAIN AND CORD.

After hardening in formalin the brain was stripped of its membranes. The middle cerebral artery and its branches, as far as practicable, were removed for microscopical examination, from the left side. The weight of the brain thus stripped was 1,245 gm.; the cerebrum alone weighed 1,080 gm., the cerebellum, pons and medulla together 165 gm.

The cerebral hemispheres were well developed and of good convolutional

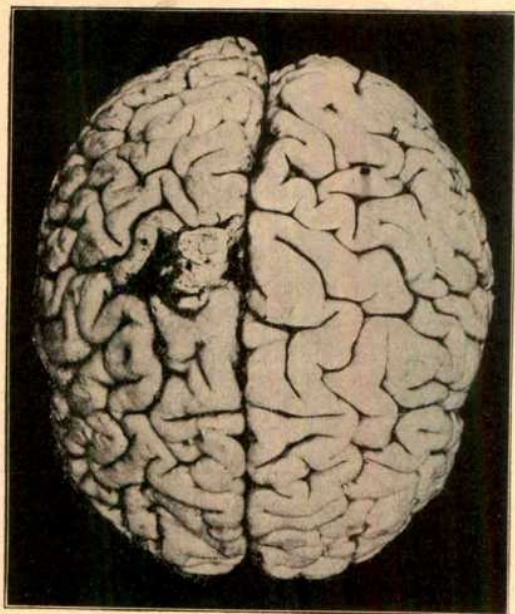


FIG. 62.—Upper surface of cerebrum (Case 3). (The membranes have been left at one spot over the right Rolandic area for histological purposes.)

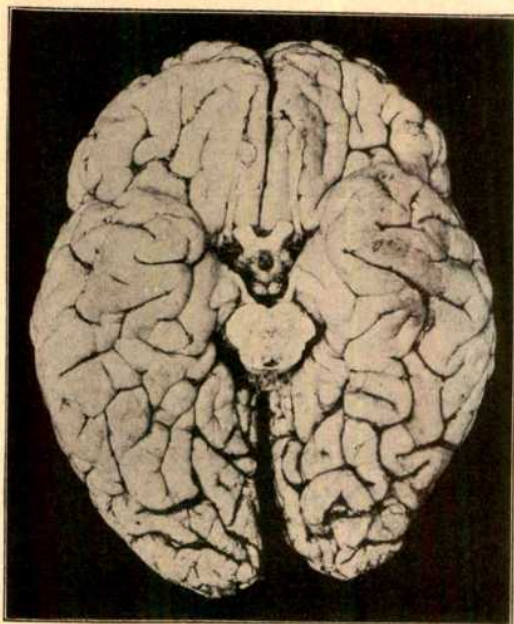


FIG. 63.—Under surface of cerebral hemispheres (Case 3). Cerebellum, pons, and medulla have been removed.

pattern, as can be seen from figs. 62, 63, and 64. There was no obvious atrophy of any of the gyri, and no undue spacing between them. The corpus callosum was divided by an incision in the mesial plane, and then each of the hemispheres was cut by Pierre Marie's *coupe d'élection*. The appearance of the sections is given in fig. 65.

Right side.—The posterior two-thirds of the putamen in its complete transverse extent, and to a less degree the corresponding part of the middle zone of the lenticular nucleus, were the seat of an obvious softening. The substance of the nucleus was discoloured, friable, pitted, as it were worm-eaten. There were a number of small holes in it, evidently related to blood-vessels; many were clean cut and empty, and round these—i.e., in the area where these were—the degeneration of the nucleus seemed at its maximum. The minute vessels which remained stood out from the surface of the section, were patent,

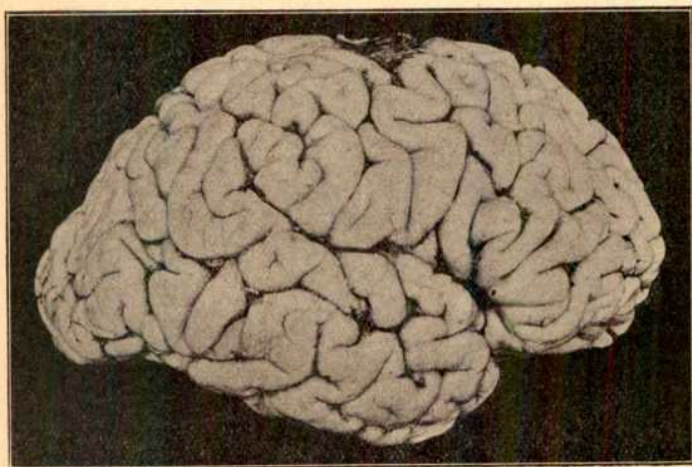


FIG. 64.—Right hemisphere (Case 3).

tore very easily, and when extracted left a small but gaping hole behind. The whole substance of the nucleus in the affected area was greatly shrunk, slightly hollowed out, and clearly in an early stage of definite cavitation. The diameter of the minute punched-out holes averaged 1 to $1\frac{1}{2}$ mm.; the length of the degenerated area was $2\frac{1}{4}$ cm., and its greatest breadth $\frac{3}{4}$ cm.

The degenerated area also included the middle third of the external capsule, so that its white fibres no longer stood out clearly between the claustrum and the outer zone of the lenticular nucleus. The claustrum itself appeared normal. The inner zone of the lenticular nucleus (*globus pallidus*) was certainly somewhat shrunk, but did not look degenerated, while the internal capsule was intact throughout its whole extent. The cortex of the island of Reil looked normal.

Even with the naked eye it was easy to determine that the fine internuncial fibres, so conspicuous a feature of the zones of the lenticular nucleus, had to a large extent disappeared, especially in the area of degeneration. The

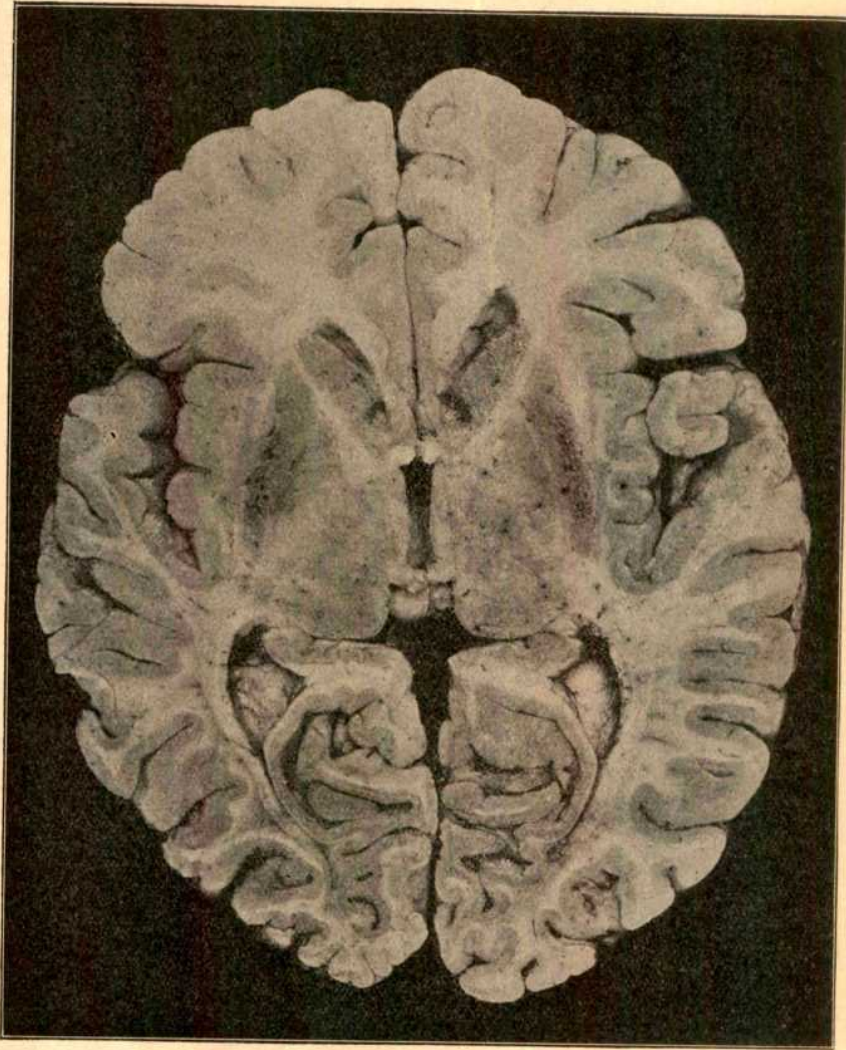


FIG. 65.—*Coupe d'élection* of hemispheres (Case 3). Bilateral symmetrical degeneration and atrophy of lenticular nuclei. Note integrity of internal capsules and normal thalami.

outer lamina could scarcely be distinguished, while the inner lamina, also between the middle and the internal zones, was very indistinct.

There was no other visible abnormality on the transverse section of this hemisphere. The caudate nucleus was possibly in a slightly atrophic state. The optic thalamus appeared perfectly normal.

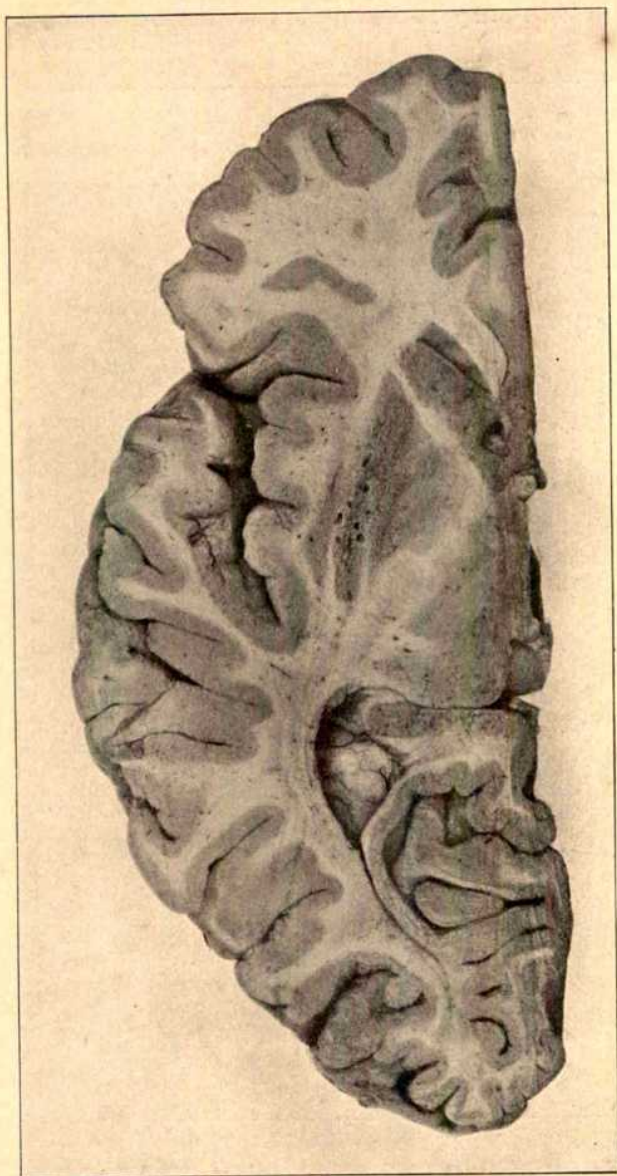


FIG. 66.—*Coupe d'élection*, left hemisphere (Case 3). Atrophic degeneration of lenticular nucleus. Compare in detail with fig. 67.

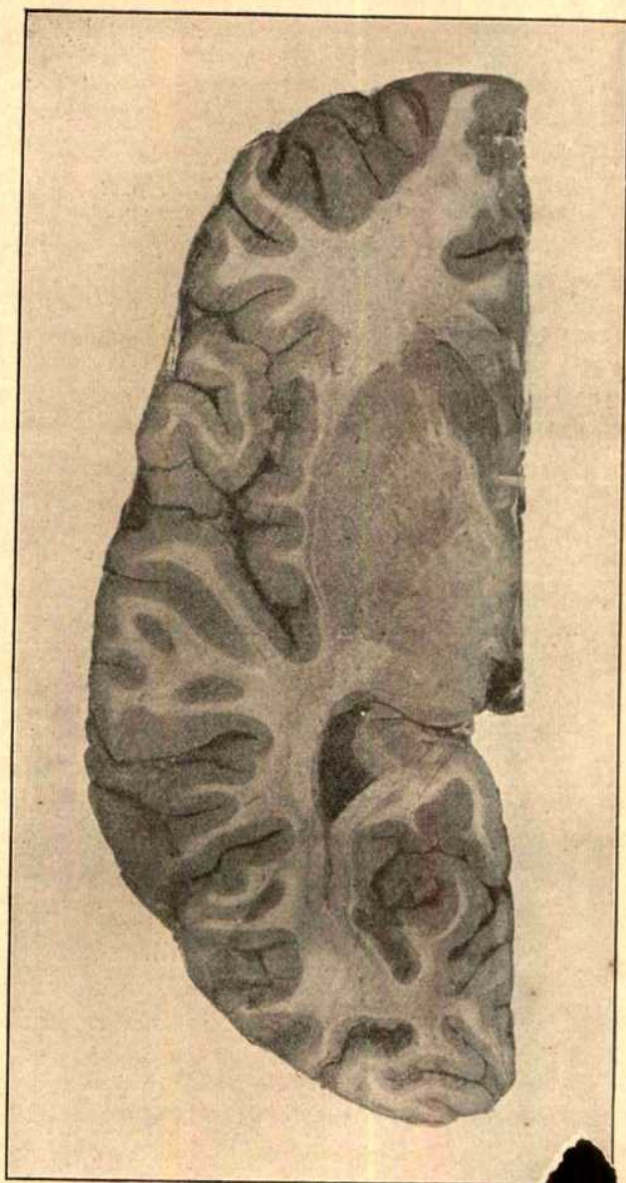


FIG. 67.—*Coupe d'élection*. Normal brain of a youth who died of the liver without nervous symptoms. Note full rounded cornu of the lateral ventricle. Compare in detail with fig. 66.

Left side.—The condition on the left side was remarkably like what obtained on the right. The situation, shape and appearance of the affected area, the slight cavitation, the punched-out little holes, were identical. The affected area presented the same discoloration, felt soft and friable, and was clearly in a state of disintegration. The globus pallidus, in its mesial zone, seemed normal and felt less soft to the touch, but it was somewhat shrunken. There was the same disappearance of internuncial fibres and laminal fibres on the left side, as well as a slight involvement of the middle part of the external capsule. Otherwise there was no change to be noticed. The caudate nucleus and optic thalamus appeared normal; the internal capsule was entirely unaffected.

The affected area on this side had the following dimensions: $2\frac{1}{4}$ to $2\frac{1}{2}$ cm. long by 1 to $1\frac{1}{4}$ cm. broad.

There was no hydrocephalus and no ependymitis. Possibly the white matter of the occipital lobes was a little less ample than it ought to have been. The cortex of the frontal convolutions on both sides, the white matter of the frontal lobes, and briefly the whole of the visible cortex, appeared of good depth everywhere.

It is important to compare the naked-eye appearances on this section of the hemispheres of Case 3 with the appearance in the normal brain from a case of cirrhosis of the liver, in a youth, in whom there were no nervous system symptoms.¹

Fig. 66 represents the left hemisphere of Case 3. The optic thalamus is seen to be as well developed as in the normal brain; the caudate nucleus is perhaps a little small; but the lenticular nucleus is grossly shrunken and atrophic, especially the putamen; its outer contour is no longer rounded and full, but is straighter, in fact, concave at one place; it is darker in colour than in the normal state, is perforated with holes, and has lost its laminal and internuncial striation to a great extent; the external capsule is thinned, and the white matter of the convolutions of the island of Reil looks a little less distinct than it should, although it does not appear to be wasted. The internal capsule (anterior and posterior limbs) is perfectly preserved.

Fig. 67 represents the *coupe d'élection* of the left hemisphere in the case of a boy who died from cirrhosis of the liver, without any nervous symptoms at death. It shows a normal corpus striatum, with a full rounded contour. The contrast between it and the previous figure is very impressive. The atrophy of the lenticular nucleus in progressive cirrhosis of the liver becomes in this way strikingly apparent.

¹ Taken from a paper contributed to Dr. T. R. Elliott and Dr. Otto May, of University

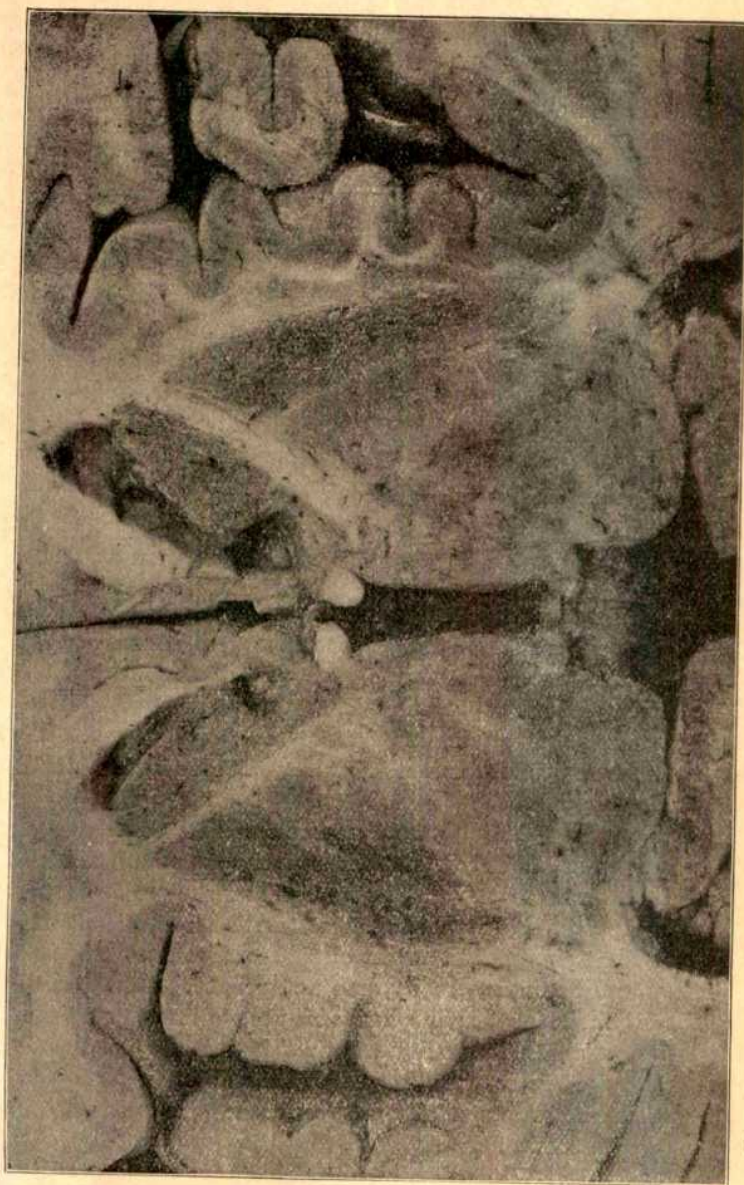


FIG. 68.—*Coupe d'élection*, hemispheres (Case 3). Soft, friable, disintegrated nucleus lenticularis on each side. (About $\times 2$.)

A photograph taken with a higher magnification (fig. 68) shows that the caudate nucleus has retained its fibre-striation in a normal way, whereas the striation of the lenticular nucleus is most defective. It also shows that the globus pallidus is less disintegrated than the putamen, and that the internal capsule and optic thalamus on each side are unaffected to the naked eye.

MICROSCOPICAL EXAMINATION OF THE CENTRAL NERVOUS SYSTEM.

On microscopical examination the cord did not present any noteworthy feature. It was of good size on transverse section at various levels, and presented no sign of degeneration. The membranes were not thickened except that the pia-arachnoid looked a little "milky" in one or two places.

(1) *Muscles*.—Sections were embedded and cut in celloidin, and stained by hæmatoxylin-eosin, Van Gieson-Pal's method for intramuscular nerves, counterstained with cochineal.

The chief change was that the muscle-fibres were in many places rounded, instead of being polygonal, and were somewhat separated from each other instead of being closely packed. There was a commencing but still slight interstitial change in many of the sections examined; the muscle-fibres were surrounded by narrow strands of connective tissue with multiplying nuclei. In some places there was increase of nuclei in the sheath of the fibres, but, speaking generally, these changes were nowhere advanced. Many parts of the muscles were indistinguishable from the normal. There were no hypertrophied fibres, and none markedly atrophied. They were all about the same size. The fibres stained well; no alteration in sarcoplasm or myoplasm was discoverable. The muscle-spindles seemed normal. The intramuscular nerves were not obviously changed.

(2) *Peripheral nerves*.—These were not separately examined.

(3) *Spinal cord*.—For the cord the methods utilized were Marchi, Weigert, Weigert-Pal, Nissl, hæmatoxylin-Van Gieson, hæmatoxylin-eosin.

To take the methods for the myelinated fibres first: The sections stained by Marchi's method, from six different levels of the cord, were negative. There was no indication of degeneration, beyond the presence of a few discrete granules, in any of the columns; in particular, the pyramidal tracts, crossed and direct, and the descending anterolateral tracts from the brain-stem, showed no change. Of course, the illness had been of some years' duration, but on the other hand it was essentially progressive, so that the negative result with Marchi is of significance.

The sections stained by Weigert's original method, of which a series is given in figs. 69 to 71, were equally negative. There was no trace of any degeneration in the corticospinal tracts, from the upper to the lower extremity of the cord. The same result was obtained by Pal's method. The columns were all of good size, and stained deeply. There was in some places an indication of

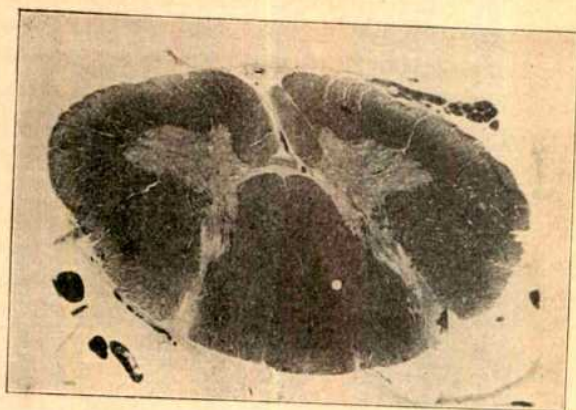


FIG. 69.—Cervical cord (Case 3). Weigert.

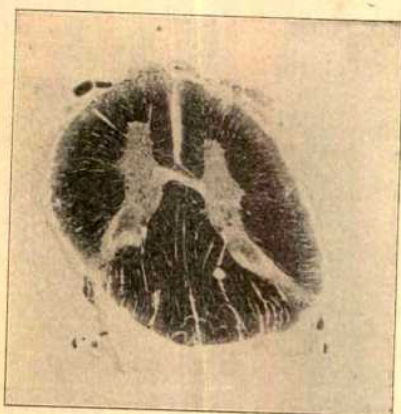


FIG. 70.—Dorsal cord (Case 3). Weigert.

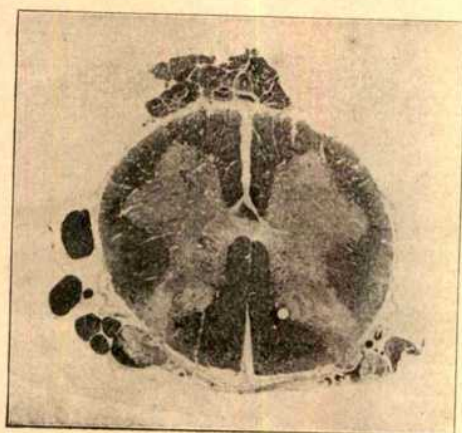


FIG. 71.—Lumbar cord (Case 3). Weigert.

slight peripheral loss of fibres round the margin of the cord, but this was very sparse. The myelinated fibres of the grey matter of the cord stained normally.

With Nissl's method (thionin blue) the anterior horn motor cells were carefully examined at various levels. (Figs. 72, 73.) There was scarcely any loss of cells. In all the sections they were present in good numbers, preserving their ordinary grouping; as a rule they were of good size and shape, and stained well. On the other hand, it was clear that some had undergone a change which is well portrayed in fig. 73. This change is one which is frequently met with in disease of a chronic and progressive nature associated with helplessness and with muscular weakness, for instance, an advancing case of tabes. It consists in a slight shrinkage of the achromatic part of the cell protoplasm, so that the Nissl granules are closely packed together, and the cell, therefore, stains darkly. It is often elongated, and its processes may be less straight than they usually are. But it does not lose its nucleus; the latter remains nucleolated, and it, too, often takes on the stain more deeply. Such cells were often met with in the Nissl sections of the cord. Others showed some pigmentary degeneration: others, again, showed commencing degenerative changes of a less chronic type, in which the tigroid substance becomes more finely granulated, specially round the nucleus, and stains less well, while the nuclear membrane disappears.

Such as they were, the changes may be said to indicate the results of long-continued imperfect use of the musculature, without signifying any definite local atrophic change. Perhaps some of the more acutely altering cells were associated with the effects of a terminal infection.

With ordinary tissue stains it was seen that some leptomeningitis was present, but this was nowhere severe. It was irregularly distributed over the cord, but the significant fact in regard to it was the absence of anything like small-cell infiltration of the meninges. The blood-vessels of the cord, the anterior spinal artery and the intramedullary arterioles, were normal. There was no trace of endarteritis.

(4) *Medulla oblongata and pons*.—The same methods were utilized for these as for the cord.

With Pal's stain for medullated fibres no obvious change could be discovered. The pyramids stained deeply, and were not atrophic in any way; the olives, restiform bodies, fillet, &c., all appeared normal. In the pons there was no change that could be described as pathological.

The sections stained by Marchi's method were not so successful; prolonged immersion of the tissues in formalin militates against good results. No characteristic degenerations, however, were found.

In view of the patient's condition during life the nuclei of the lower cranial nerves were specially examined by Nissl's method. A description of the cells of the hypoglossal nucleus will suffice. If the reader will look at fig. 74 he will see that there is no loss of cells; in other words, the condition is very different from an ordinary bulbar paralysis. The cells stained well and deeply, and the majority were of good shape; others showed the same

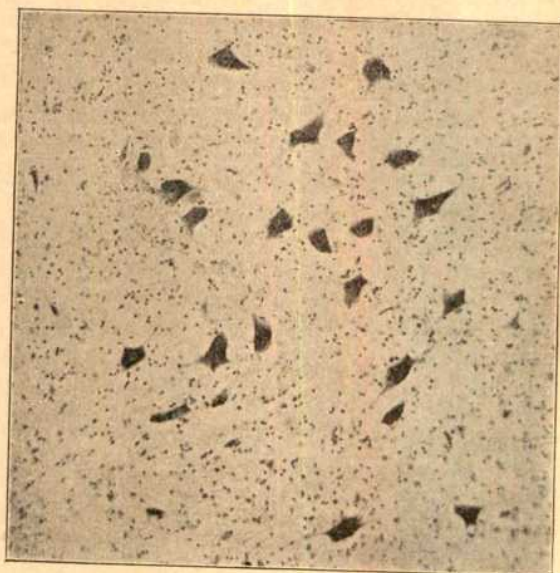


FIG. 72.—Anterior horn-cells, lumbar cord (Case 3). Nissl.

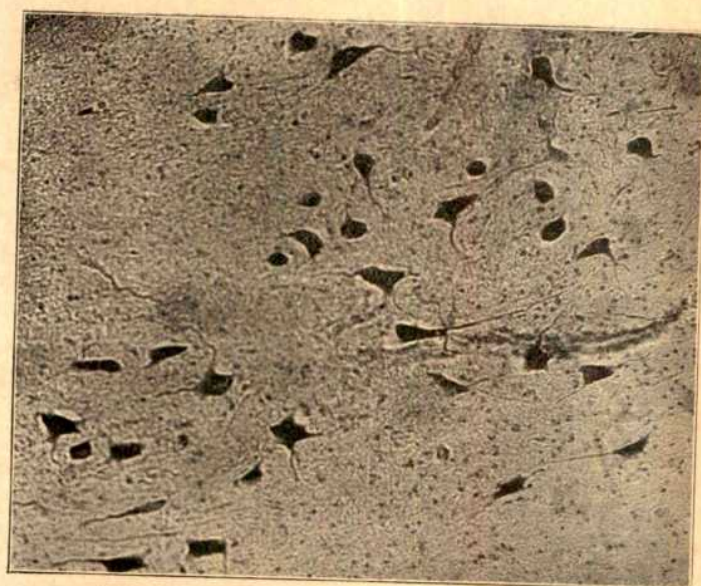


FIG. 73.—Anterior horn-cells, cervical cord (Case 3). Nissl.

elongated and "intensified" appearance that has been already noted in the spinal cord.

The cells of the facial and other motor nuclei were similarly numerous, not atrophic, and many showed the changes that have just been described. Round a few of the nuclear cells parasite glial cells were found.

(5) *Cerebellum*.—The cells and fibres of this organ seemed quite normal with the same stains as for the cord. The Purkinje-cells, granular layer, dentate and other nuclei, presented no departure from similar sections of a normal case used as a control.

(6) *Crus*.—Weigert and Weigert-Pal sections of the crus cerebri (fig. 75)

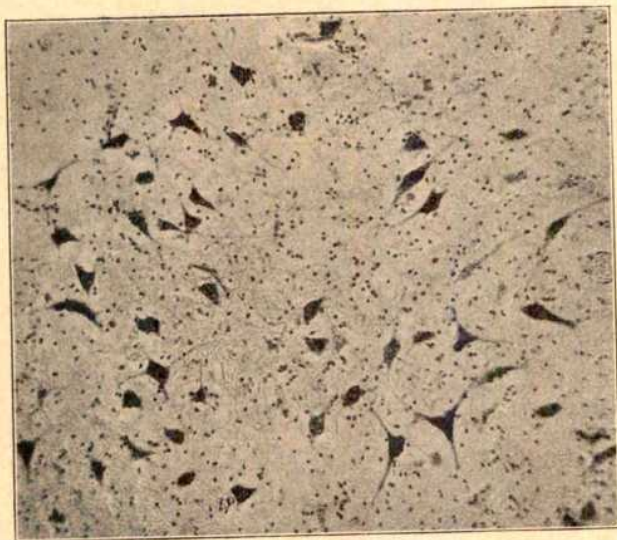


FIG. 74.—Right hypoglossal nucleus (Case 3). Nissl. Notice that there is no loss of cells.

were in every respect normal. The pyramidal fibres were apparently intact, stained well, and were not diminished in quantity, compared with similar sections from a normal brain. The components of the crus on either side of the pyramidal tract were unaffected. The substantia nigra was not obviously altered. The tegmentum was not deficient in any way. The fibre-content of the nucleus ruber seemed normal.

With Nissl's method the cells of the nucleus ruber were examined. They were not diminished in number; most of them stained well, and were of normal shape. Not a few stained rather poorly, while still preserving their shape. Round many of them were parasite neuroglial cells in considerable numbers (fig. 76)—a condition which is almost certainly indicative of failing nutrition of the nerve-cells, from excessive functionary, or from other causes.

(7) *Basal ganglia, internal capsule, and subthalamic region*.—On the right side the central part of the hemisphere was cut into slabs by a series

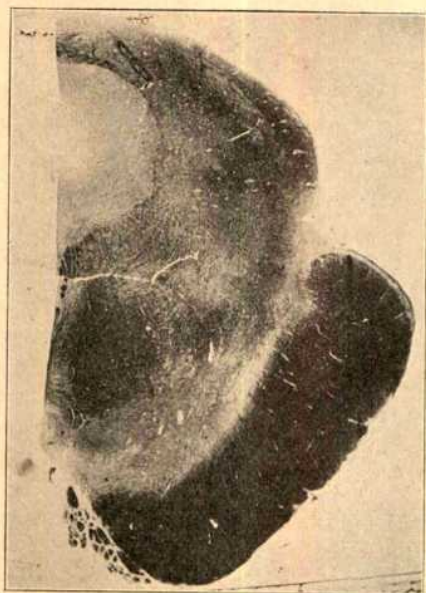


FIG. 75.—Crus cerebri (Case 3). Weigert. Normal appearance.

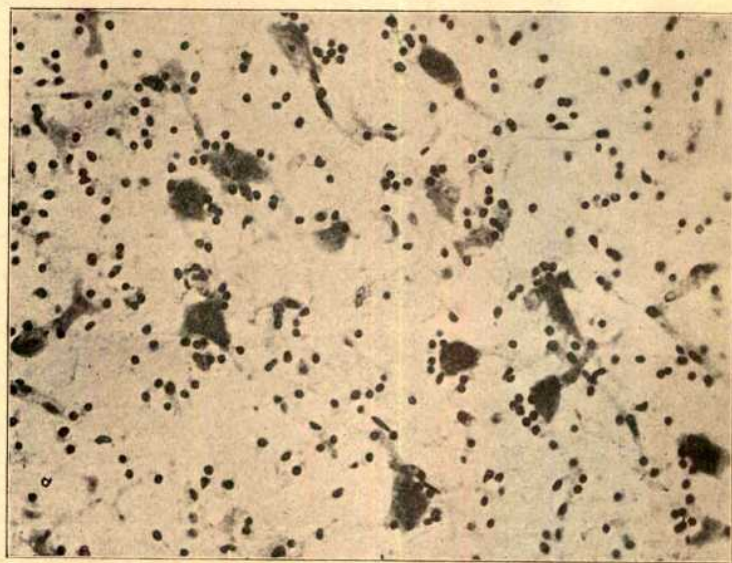
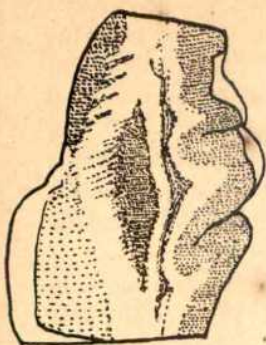
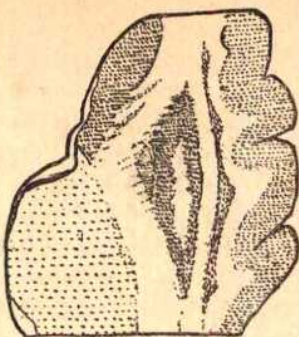


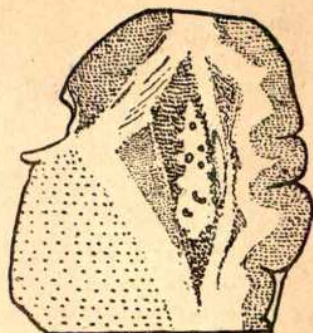
FIG. 76.—Cells of red nucleus (Case 3). Nissl. Numbers of parasitic glial cells round many of the nerve-cells.



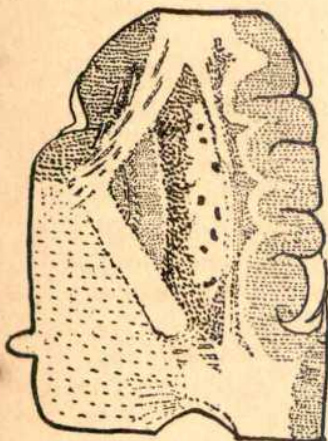
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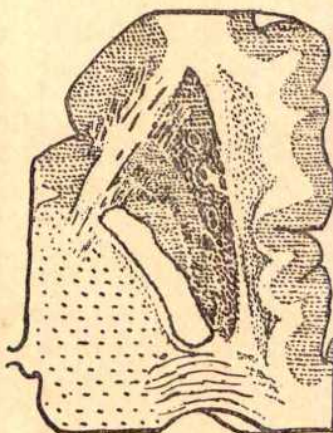
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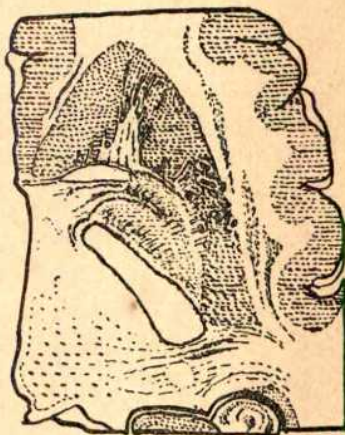
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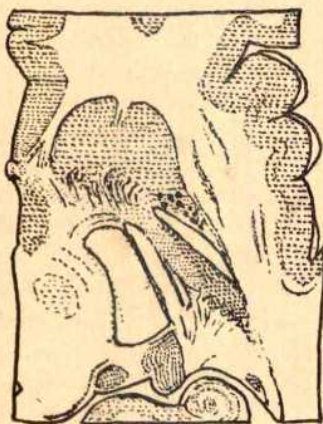
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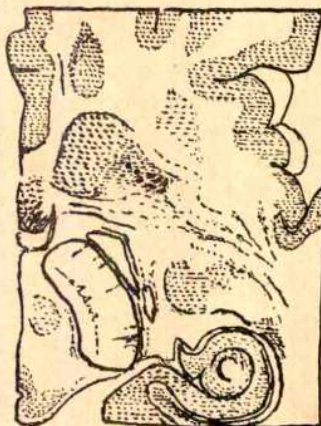
No. 5.



No. 6.



No. 7.



No. 8.

FIG. 77.—Drawings of cut slabs of right basal ganglia (Case 3). Natural size. For description see text.

of incisions exactly parallel to the *coupe d'élection*. Some of these were taken for Nissl and ordinary tissue stains, others were placed in Müller's solution for Pal and Weigert. On the left side similar slabs were cut; some were utilized for Marchi, others for a Weigert-Pal series of the subthalamic region.

(a) *Minute anatomy of the lenticular degeneration*.—The accompanying series of drawings represents the appearance of the upper aspect of the cut slabs of the right hemisphere, from above downwards, and serves to give, as it were, a reconstruction of the lenticular degeneration.

No. 1 represents the putamen above the level of any visible degeneration, with a normal internal and external capsule, claustrum, &c. In No. 2 the area of disease has made its appearance, and is seen to occupy a somewhat crescent-shaped strip of the putamen, towards its outer side, while the beginning of the middle zone (globus pallidus) just appears to its inner side. The external capsule appears intact. In No. 3 the affected area is broader, occupies posteriorly almost the whole breadth of the putamen, touches the external capsule slightly, and contains in its centre the gaping holes round the lenticulo-striate vessels that have already been mentioned. No. 4 shows the appearance at the *coupe d'élection*, and corresponds to the photograph reproduced as fig. 65. No. 5, a little lower, still shows clearly how the degeneration is related to the lenticulo-striate vessels; it appears to be confined at this level to the putamen. The globus pallidus appears unaffected, at least directly. Further down, through Nos. 6, 7, and 8, there is no degeneration to be seen by the naked eye, and where the lenticulo-striate vessels enter the brain they appear to be normal, nor is there any recognizable area of softening round them.

In the sections stained with hæmatoxylin-eosin, under a low power, there was found a broad strip, occupying almost the whole of the putamen, which stood out prominently and unmistakably. Here there was a pronounced degree of sclerotic change, consisting in a great overgrowth of neuroglia, which in a number of places was commencing to break down. The internuncial fibres from the putamen could not be distinguished; the nerve-cells of the nucleus were few and far between. In and round this area the blood-vessels were somewhat dilated, with widening of the space of Virchow-Robin around them, occasioned probably by retraction of the tissues under the action of sclerosis. Towards the periphery of the degenerated area the sclerosis was densest, towards its centre it was thinner, and there the tissue was commencing to break down; no doubt more cavitation would have ensued had the patient lived longer. Fig. 78 gives an idea of this low-power appearance.

With a higher magnification this whole area was seen to be a confused mass of neuroglial overgrowth and tortuous small vessels, forming an amorphous network in which the true nerve-elements of the nucleus were lost. Fig. 80 gives an excellent impression of the density of this change in the putamen, and illustrates well the amorphous character of the degeneration.

Under a still higher magnification (fig. 81) it was noted that the nerve-cells of the putamen had almost entirely disappeared; only a few could be discovered.

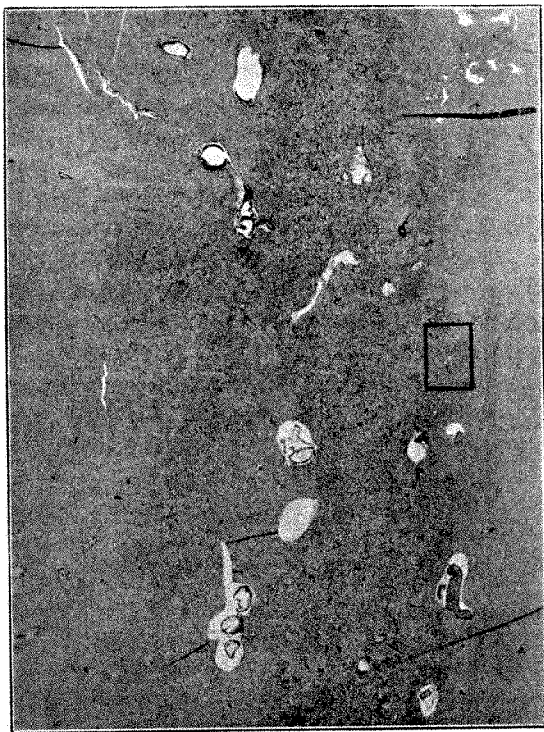


FIG. 78.—Degenerated area of right putamen (Case 3). For key see fig. 79. = fig. 80.

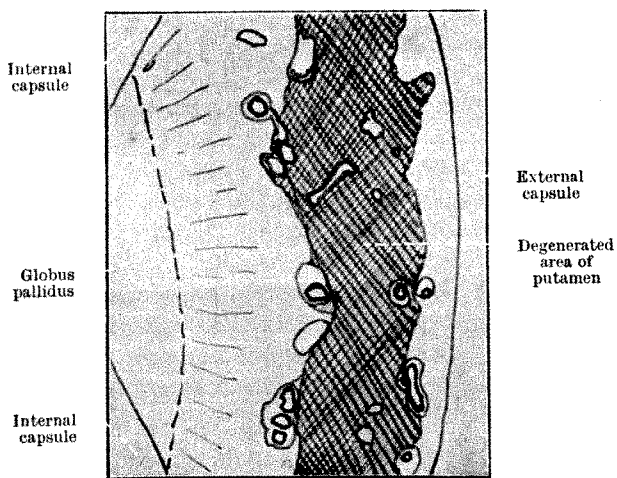


FIG. 79.—Key to fig. 78.

Neuroglial nuclei and cells and fibres formed the chief feature in the picture. In some places they were actively growing; in others they were sparse, where the tissue was breaking down. Everywhere numbers of the so-called "Körnchenzellen" could be seen. Such nerve-cells of the putamen as were left were usually shrunken and stained very deeply. With Marchi's method some of the few nerve-cells that remained were found to be full of minute fat-granules. The bundles of internuncial fibres leaving the putamen to enter the globus pallidus were very difficult to trace.

The condition of the blood-vessels deserves special attention. As has already been remarked, under a low power, so far from being thickened or obliterated, they were if anything thinned and dilated. The wide spaces

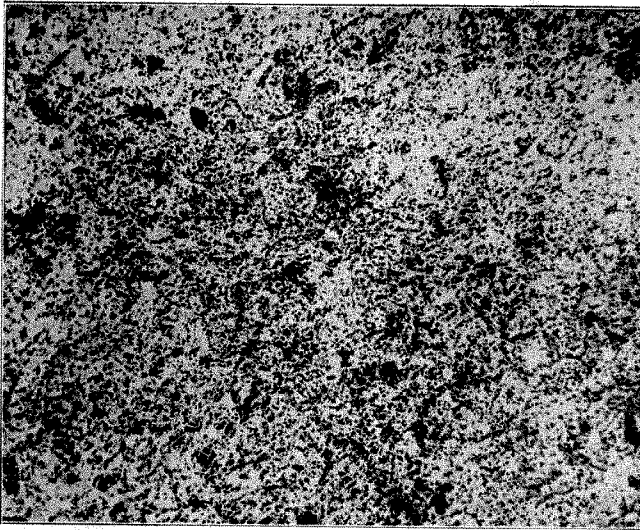


FIG. 80.—Degenerated area, right putamen (Case 3). Hæmatoxylin-eosin. A mass of amorphous neuroglial overgrowth, breaking down in some places. ($\times 60$.)

surrounding them were mostly empty; the margins were formed of a feltwork of neuroglia. Towards the centre of the diseased area, however, the same spacing was not remarked, and there was a considerable degree of disintegration round the vessels. Under a higher power there was no trace of any small-cell infiltration that would suggest an inflammatory reaction. The lymphatic sheaths of the vessels were somewhat dilated, but they did not contain small round cells. The coats of the lenticulo-striate arteries could be seen to be of normal proportions; in no single vessel was there any endarteritis; the elastic lamina was mostly intact, the muscular layer was a little thinned or stretched, the adventitia was in some instances perhaps a little thickened. The arterioles and capillaries, also, were free from any sign of

endarteritis. In scores of sections I failed to discover a single obliterated vessel. (Fig. 82.)

Compared with the putamen, the cells of the globus pallidus were less interfered with, though still much diminished; this section of the nucleus lenticularis showed little change (with hæmatoxylin-eosin), beyond increase in neuroglial nuclei and a general increase in the density of its tissues. Similarly the cells of the claustrum revealed little, if any, pathological change, and its neuroglial groundwork was practically normal.

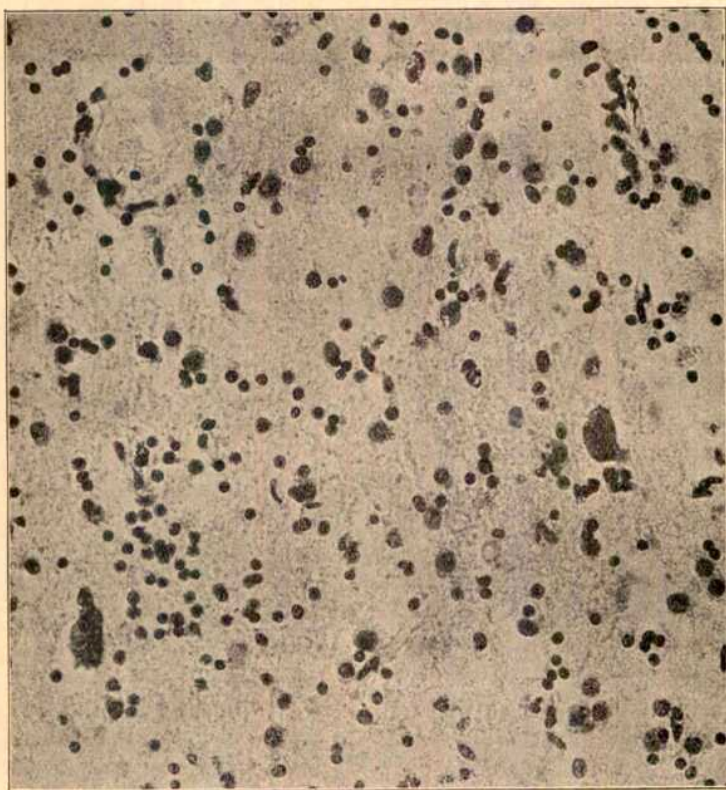


FIG. 81.—Degenerated area, right putamen (Case 3). Nissl. ($\times 500$.) Two degenerated nerve-cells, neuroglial cells, "Körnchenzellen," &c. Tissue breaking down.

Sections from the degenerated portion of the lenticular nucleus, stained with osmic acid, showed the presence of great numbers of large round phagocytic cells crammed full with fatty granular debris, but only where the tissues were actually disintegrating. Round the edges, where the neuroglial overgrowth was densest, these cells were not found. (Fig. 83.)

(b) *Optic thalamus and caudate nucleus*.—No changes in these ganglia, analogous to what obtained in the putamen, could be found. The cells of the

different nuclei of the thalamus (anterior, external, ventral) were for all practical purposes normal, and similarly with the cells of the caudate. There were no neuroglial changes that could be distinguished with certainty.

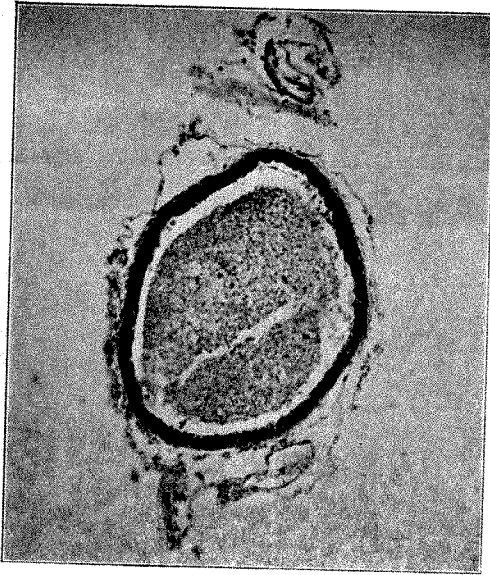


FIG. 82.—A single minute lenticulo-striate vessel, removed and cut separately (Case 3). Hematoxylin-Van Gieson. It is, if anything, thinned. No trace of endarteritis.

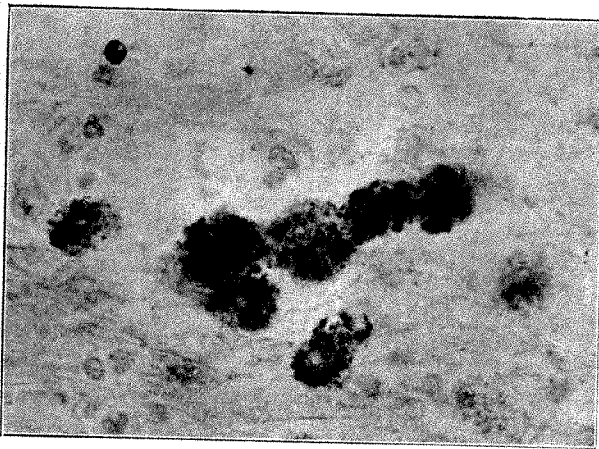


FIG. 83.—Macrophages from the degenerating area, left lenticular nucleus (Case 3). Marchi. They are crammed with fatty granular debris.

(c) *Internal capsule and fibres of the corpus striatum.*—By the methods of Weigert and of Weigert-Pal the fibre-content of the basal ganglia was investigated.

In a series of sections cut consecutively from above downwards it was seen that the maximum of defect was in the middle third of the putamen, regarded vertically, and to a less extent in the upper third; in the lower third, however, there was also a profound fibre-defect.

In a section at the level of the upper part of the corpus striatum the internal capsule was perfectly normal, and the pencils of fine fibres passing from the putamen mesially were also normal. A little lower, at the level of the upper margin of the globus pallidus (fig. 84), disintegration commenced



FIG. 84.—Horizontal section, right hemisphere (Case 3). Weigert. Note integrity of internal capsule and optic thalamus, normal fibre-content of caudate, atrophic degeneration of putamen, and of globus pallidus (to a less extent). Note also slightly imperfect external capsule.

in the putamen, in its middle third. There, the pencils of internuncial fibres were atrophic, and many had disappeared; at the anterior and posterior extremities of the nucleus, however, they were still in evidence. The outer margin of the putamen, instead of being rounded, was in two places concave, indicating considerable loss of substance. The external capsule at these two places was itself thinned, and took the stain feebly. At the level of the middle of the globus pallidus, regarded vertically, there was much atrophic change in the putamen, both as regards its size and its fibres. The external lamina was very incomplete. The external capsule was defective, as noted

already. The inner lamina was also defective and the fibres passing from the middle to the inner segment of the lenticular nucleus, though present in fair numbers, stained much less well than normally. The fine fibres coming across the anterior limb of the internal capsule, from the caudate to the putamen, stained well, and did not appear obviously reduced in numbers. The internal capsule was unaffected throughout. The fibres underlying the convolutions of the island of Reil were not involved.



FIG. 85.—Horizontal section, right hemisphere (Case 3). Weigert. Grossly atrophic putamen and globus pallidus. Compare in detail with a corresponding section from a normal brain (fig. 86).

At a still lower level (fig. 85) the atrophy of the shrunken putamen was very apparent. It was riddled by small holes, some of which were confluent, notably along the outer margin of the nucleus. Its fine fibres were almost all diseased. The laminae of the nucleus were greatly degenerated, and in



FIG. 86.—Section of normal brain corresponding to that of fig. 85, Weigert. Note in particular the normally staining globus pallidus and laminal and internuncial fibres.

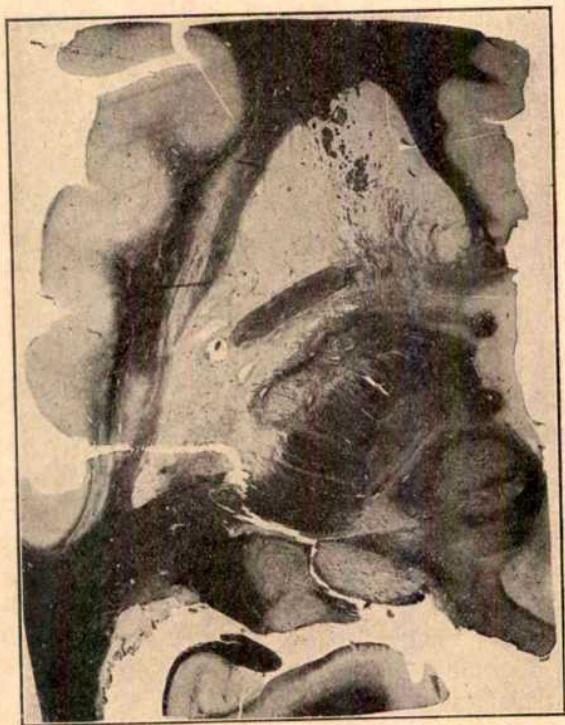


FIG 87.—Subthalamic region, left hemisphere (Case 3). Weigert. (About $\frac{3}{4}$.) Description in text.

particular the fine fibres of the globus pallidus were affected to such an extent that they could scarcely be traced. If the appearance in this figure is compared with that of a normal brain taken at the same level, the contrast between the healthy and the degenerated globus pallidus is very noticeable (fig. 86). The external capsule was as described above.

In the subthalamic region (figs. 87 and 88) it could be seen that the ansa lenticularis, where it sweeps round the crus, was partly affected; it did not stain so deeply as some of the neighbouring structures, nevertheless it still contained a number of apparently healthy fibres. The strio-Luysian fibres could be readily distinguished; many were degenerated, but probably an equal number seemed normal. No doubt, some at least of these were passing in the reverse



FIG. 88.—Horizontal section, right crus, somewhat lower than that of fig. 87 (Case 3). Weigert. Description in text.

direction. The prolongation of the ansa lenticularis to the capsule of the red nucleus (Dejerine) could not be followed satisfactorily. The lenticular bundle of Forel was slightly degenerated. The corpus Luysii was somewhat smaller than normal, and on the whole its fibres stained rather less well than usually; nevertheless, on microscopical examination only relatively few diseased fibres could be found in it. The zona incerta did not appear obviously altered, except that perhaps it was a little smaller than in sections from a control brain. The field of Forel stained normally. Further back, its place is taken by the red nucleus, which in the present case was not apparently defective in any way.

The fibres in the external segment of the optic thalamus, and those crossing the capsule from the corpus striatum to that part of the thalamus, were slightly reduced in numbers, but most of them took the stain deeply. The

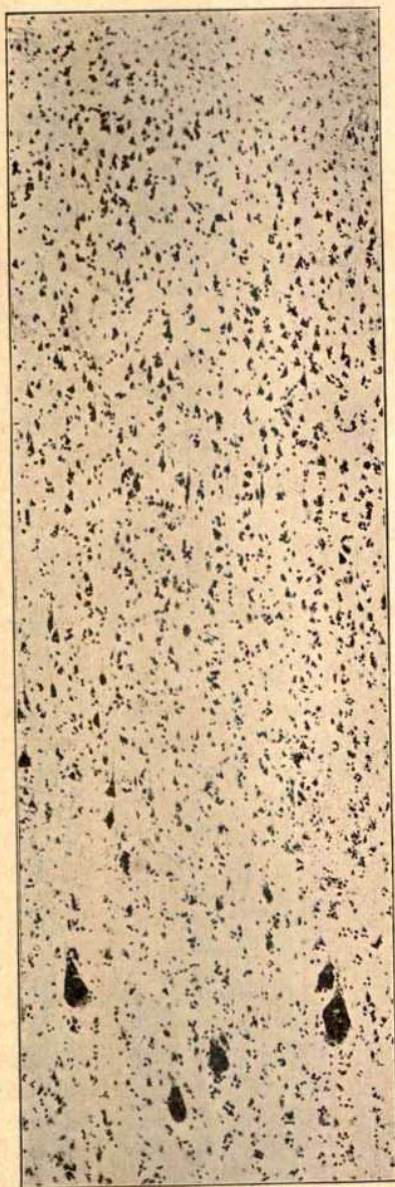


FIG. 89.—Strip from precentral gyrus, left leg centre (Case 3). Nissl. Normal Betz-cells.

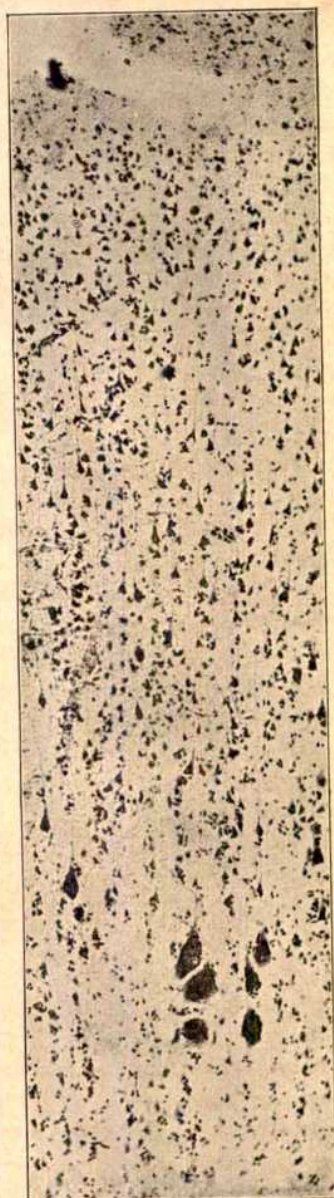


FIG. 90.—Strip from precentral gyrus left arm centre (Case 3). Nissl. Normal Betz-cells.

"zone grillagée" and the external medullary lamina of the thalamus were not altered to any great extent.

The whole of the subthalamic region on the left side was cut in serial section by Marchi's method, but no positive change was discovered except that the ansa was definitely though not profoundly degenerated. The staining, however, owing no doubt to the tissues having been in formalin so long, was not perfect.

(8) *Cortex cerebri*.—The left motor area was investigated by a series of pieces taken from it, to include both the precentral and the postcentral convolutions. In addition, the cortex of the island of Reil, as well as of the posterior and of the third left frontal convolution, was examined. Special attention was given to that part of the motor area, at the lower end of the precentral gyrus (operculum), from which originate the fibres that innervate the muscles of articulation, via the bulbar nuclei.

Figs. 89 and 90 represent strips of the cortex of the leg and of the arm area. There was, in the first place, no defect in number, or in shape and staining properties, of the Betz-cells. Further, the zonal layer, outer granular layer, pyramidal layer, Betz-cell layer, and fusiform layer, could be readily distinguished, and were not obviously defective in any way. Some of the pyramidal cells showed small collections of glia-cells round them, and possibly they were slightly diminished in number.

In the other portions of the cortex examined there was little or no departure from the normal. In particular, the motor centre for articulation showed no obvious loss of cells, although here the pyramidal cells seemed in some instances to be unduly elongated and to stain too deeply.

In no one of many scores of sections was there any trace of small-cell infiltration of cortical vessels.

The fine myelinated fibres of the motor cortex were examined by the method of Pal. There was some diminution in the fibres of the tangential layer, or zonal layer. It was not so dense and well defined as in the normal brain. On the other hand, the supraradiary and intraradiary networks were apparently unaltered.

MICROSCOPICAL EXAMINATION OF OTHER ORGANS.

(i) *Liver*.—The histological methods employed were hæmatoxylin-eosin, hæmatoxylin-Van Gieson, Weigert's stain for elastic tissue, Sudan III for fat.

The liver presented a very interesting appearance under a low magnification. Its substance was divided into numerous islets of highly irregular size, most of them including perhaps six or eight lobules, or liver units. Others were so small as to include only one lobule—of these only a few were seen—and in other instances less than one lobule, in fact only a few liver-cells were enclosed in cirrhotic tissue. This fact was determined by the use of serial sections. Speaking generally, the cirrhosis was of mixed but mainly multilobular type. Round the islets was cirrhotic tissue in abundance, of varying breadth, much

more cellular than fibrous, on the whole, and containing numerous young connective tissue corpuscles. A very prominent feature of the cirrhotic strands was the presence of so-called hypertrophying bile-ducts. In some places these were almost the only structures that could be seen in the field. There was little sign of intralobular cirrhosis; in a few places strands of connective tissue appeared to be dividing up the columns of liver-cells, but there was so little of this change as to be negligible.

The curious feature of the cirrhosis was its pronounced irregularity as far as its effects on the liver-cells were concerned. While many lobules were

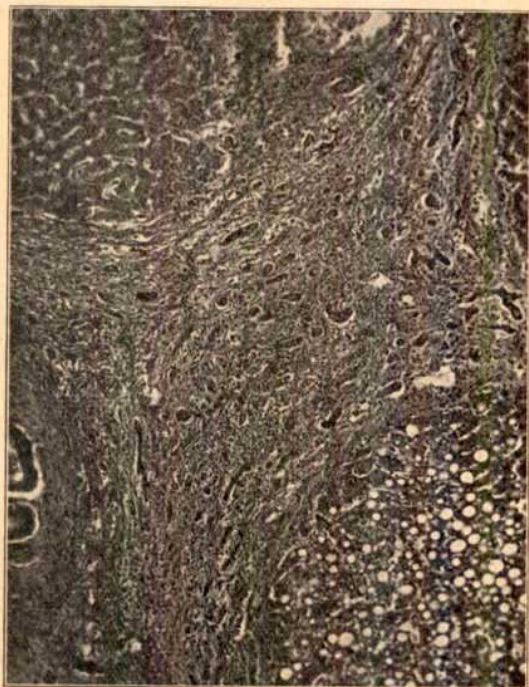


FIG. 91.—Liver (Case 3). Hematoxylin-eosin. Healthy and degenerated liver-tissue.

normal, others in their neighbourhood were not merely irregularly degenerating, but were sometimes in a state of what appeared to be acute necrosis. The whole of the centre of the lobule would be seen to be losing its cellular structure, and to be staining homogeneously, indicative of some acute chemical change. The liver-cells were in many places normal in every way; others in the same lobule might be in a state of advanced fatty degeneration. Stained with Sudan III the picture obtained was striking. Some nodules of cirrhotic tissue contained only fat-cells, so to speak; others contained no fat at all.

Abundant evidence was obtained, under a high power, of active regeneration of liver-cells. In the regenerating area it was often observed that the nuclei

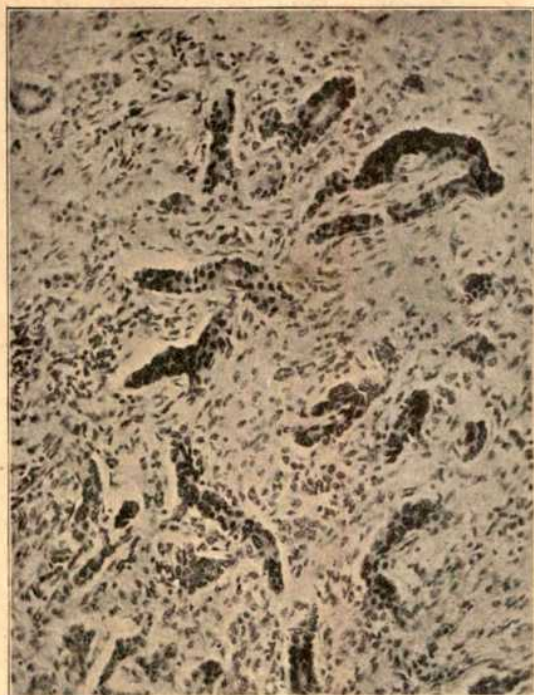


FIG. 92.—So-called hypertrophying bile-ducts in cirrhotic tissue of liver (Case 3).
Hæmatoxylin-eosin.

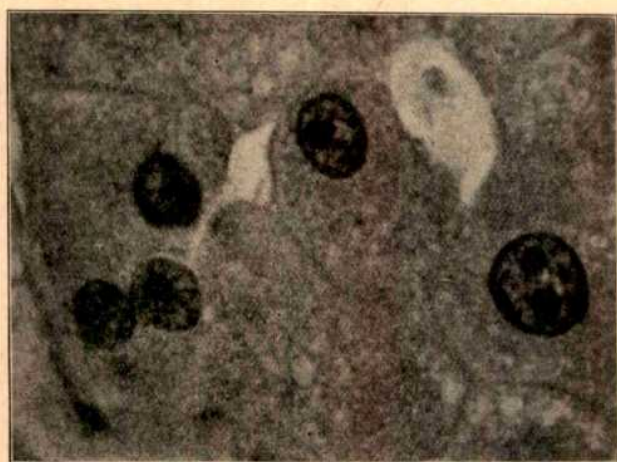


FIG. 93.—Regenerating liver-cells (Case 3). Division of nuclei. Hæmatoxylin-eosin.
($\times 1,200$.)

stained irregularly with polychrome blue, some being pinkish, others bluish; sometimes the nucleus was blue with a bright red nucleolus. Here were to be found cells undergoing amitotic division, in most instances, although a rare mitotic figure was here and there seen. Many cells had double nuclei, others hypertrophying nuclei. These varying appearances are shown in the accompanying figures (figs. 91 to 94).

One of these is instructive (fig. 94), as it shows direct continuity of the hypertrophying bile-ducts with columns of liver-cells. The portal tracts and vessels of the liver did not present any marked abnormality.

Another feature seen in the liver sections will be noted subsequently.

(ii) The other organs examined microscopically must be briefly dismissed.

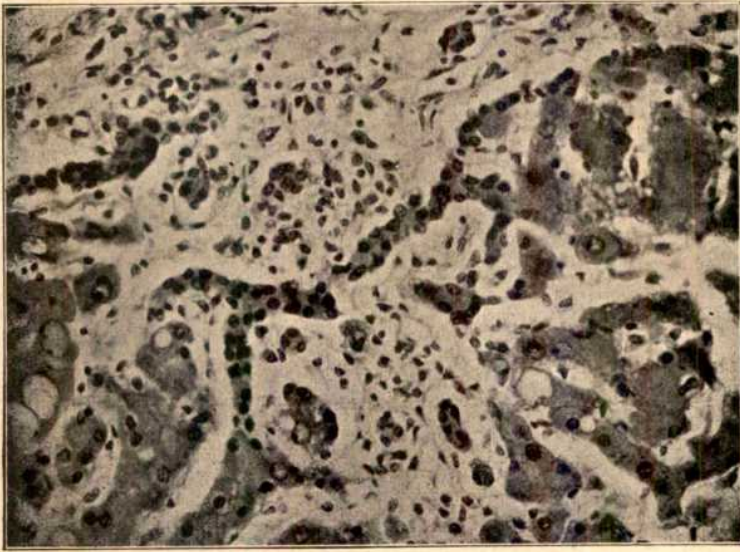


FIG. 94.—Continuity of so-called hypertrophying bile-ducts with columns of liver-cells (Case 3). Hæmatoxylin-eosin.

The thyroid showed changes such as are reproduced in fig. 95. The colloid vesicles were in many places reduced in size and number, and contained less colloid than in the normal gland. The epithelium lining the vesicles was often noticed to be in a state of proliferation. A certain amount of interstitial change was present.

The suprarenal gland did not present any unusual feature.

The thymus was of course small, but some of its tissue was persistent; it appeared to be normal.

The spleen, on microscopical examination, showed little change; what change there was indicated interstitial alteration.

The kidney did not present any unusual feature.

The pituitary also showed no obvious pathological change.

(iii) The sole remaining point in the pathology of this case of progressive lenticular degeneration is the question of a terminal infection. Scattered through the suprarenal gland, to a very much less extent in the liver, but also

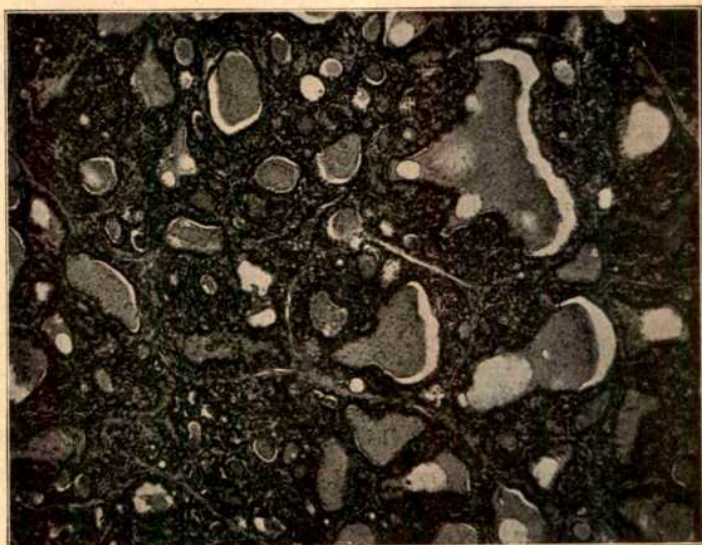


FIG. 95.—Thyroid (Case 3). Hematoxylin-Van Gieson.

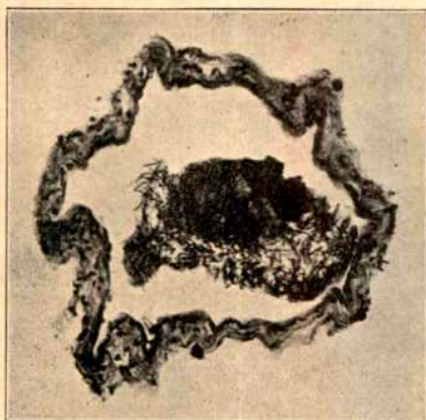


FIG. 96.—A minute vessel removed from degenerating lenticular area and cut separately (Case 3). Shows a plug of bacilli entangled in a fibrin clot. Hematoxylin-eosin.

in the brain, cord, and kidney, clumps of bacilli were here and there to be found. Fig. 96 is specially interesting, for it represents a transverse section of a minute vessel from the degenerated area in the lenticular nucleus. Entangled in the fibrin clot will be seen a mass of bacilli, stained intensely

blue-black. In view of the scattered nature of the process it is, I think, probable that its sole significance is that of a terminal infection, possibly from the alimentary canal. The bacilli resembled the *Bacillus coli* structurally, but their staining reactions seemed in one or two ways to be rather different.

RÉSUMÉ OF THE PATHOLOGICAL FINDINGS IN CASE 3.

The brain is of good size and shape, and its convolutional pattern is normal. There is no obvious atrophy of gyri, and no definite disease of the membranes, beyond slight irregular "miliness" of the arachnoid in the interpeduncular space and on the posterior aspect of the cord. The pons looks perhaps a little small in proportion.

The cerebral blood-vessels are not thickened and show no patches of disease in their walls. They are all patent.

The brain is cut open by Marie's *coupe d'élection* and at once a bilateral and strikingly symmetrical degeneration of the lenticular nucleus, in particular the putamen, meets the eye. This structure is seen to be grossly shrunken, so that its outer margin is irregularly concave, instead of being rounded and convex; it is darker in colour than normal, looks friable and feels soft, is so disintegrated that a cavity formation has begun, and is perforated by small gaping holes, in some of which the lenticulo-striate vessels, separated from the surrounding tissue, can be seen. The dimensions of the degenerated area average 3 by 1 cm. Compared with a normal brain, the lenticular nucleus is in this case considerably shorter and narrower, indicating the extent of its atrophy. The globus pallidus is less affected; the laminae and internuncial fibres between the zones of the nucleus have disappeared to a great extent in the outer section; on the inner side they are better preserved; lower down, however, the globus pallidus has undergone a great loss of fine fibres. The caudate nucleus is a little shrunken, but the optic thalamus is normal, and the internal capsule is entirely untouched.

The softened portion of the lenticular nucleus occupies approximately the middle third of the putamen, vertically considered; in the lower third there is still much shrinkage, but on the whole less disintegration. Microscopically the putamen is found to be extensively sclerosed by neuroglial overgrowth, which is breaking down in the centre; the normal cells of the nucleus have to a great extent disappeared, and numerous "Körnchenzellen" are present; macrophages abound in the degenerate area; but there is no small-cell infiltration

to indicate an inflammatory reaction, and no sign of endarteritis in the vessels of the affected region.

Although the cortex and subjacent structures of the island of Reil have the same vascular supply, they are not involved, with the exception of the middle third of the external capsule, which is thinned, and its posterior third, which is degenerated.

The cortex in the motor area, from the cyto- and myelo-architectonic points of view, is found to be normal. The pyramidal system, from the Betz-cells, through internal capsule, crus, pons, medulla, cord, anterior horn-cells, to the muscles, is exhaustively examined, but no alterations of any significance are found at all, except such as can be accounted for by the helpless and emaciated condition of the patient.

There is some degeneration in the extrapyramidal system from the lenticular nucleus via the ansa lenticularis towards the red nucleus, but the cells of the latter structure are mostly normal. Many strio-Luysian fibres are degenerated; others (some of which may be passing in a reverse direction) are normal. The corpus Luysii is rather small, and somewhat degenerated. Most of its fibres, however, stain well enough. The lenticular bundle of Forel is slightly degenerated. There is little change in the external medullary lamina of the optic thalamus, or in the "zone grillagée"; on the whole the fibres of the thalamus are well preserved.

The liver is found to be in an advanced state of cirrhosis, typically multilobular, but to some extent mixed; there is apparent increase of bile-ducts in the cirrhotic tissue, great variations in the condition of the liver-cells, many being in a condition of fatty degeneration, others normal, and others still actively regenerating, amitotic and less frequently mitotic division being seen in the last.

The spleen is slightly enlarged, but otherwise normal.

The thyroid shows interstitial changes chiefly, but there is also proliferation of epithelium.

The pituitary, thymus, and suprarenal do not present any special abnormality.

There are indications of a terminal infection in the presence of clumps of bacilli in some of the internal organs, as well as in the brain and cord.

Case 4.—The patient whose case is No. 4 is still living (December, 1911).

Case 5.—In Case 5 there was no pathological examination.

Case 6.—The autopsy was made on February 15, 1889, and is described in the notes as follows:—

"The brain-tissue was soft, probably œdematous.

"The membranes were healthy. On naked-eye examination no obvious morbid appearance could be made out.

"The spinal cord was firm; the membranes not adherent.

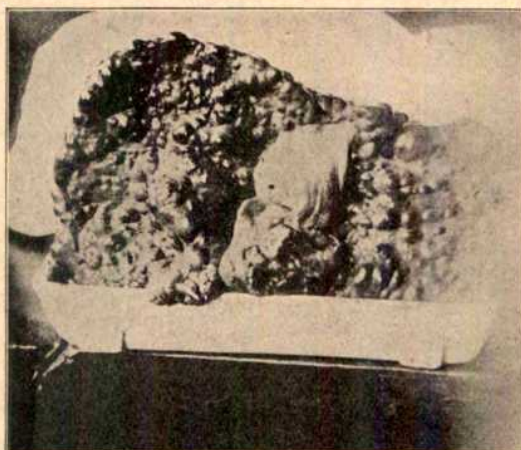


FIG. 97.—Naked-eye appearance of liver (Case 6, National Hospital, 1889).

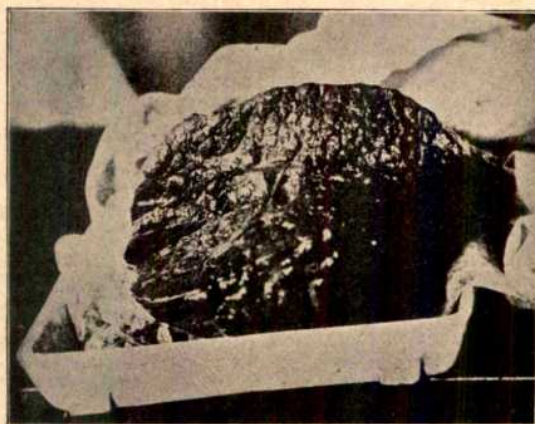


FIG. 98.—Transverse section of liver (Case 6).

"The liver was small, contracted. Small nodules, varying in size, many about the size of a small marble, all over surface. Section corresponds. Extreme cirrhosis of liver.

"Spleen large, fairly firm, much congested."

There is no record of any further examination, or of any microscopical investigation.

The appearance of the liver is reproduced as figs. 97 and 98, from the original negatives kindly lent to me by Dr. James Taylor.

CHAPTER IV.—SYNTHETIC STUDY OF THE DISEASE.

FOR the purposes of a synthetic study of progressive lenticular degeneration we have now at our disposal eleven cases, or, with the inclusion of two less certain cases, thirteen in all. Of these two, since Anton's is more doubtful than the other (my own Case 6) it will be excluded, so that this study is based on twelve recorded cases, in no fewer than ten of which an autopsy was held. Clinically and pathologically, therefore, there is abundant material for a systematized description of the disease. Of these twelve cases, six date back more than twenty years, the other six are reported in this paper for the first time.

(1) DEFINITION AND TERMINOLOGY.

"Progressive lenticular degeneration" is the nosological term with which I propose to denote the disease. Of the other terms which have been proposed, that devised by Gowers is the only one, in my opinion, which has any claim to recognition. The disadvantages of "tetanoid chorea," however, outweigh its advantages. Although pathology, where possible, should be called on to supply the name for a disease in preference to clinical medicine, the term was coined at a time when the pathology of the disease was obscure. Further, "tetanoid chorea," considered clinically, may be misleading. In the large majority of the recorded cases the involuntary movements, which form a prominent clinical symptom, are of the nature of tremor rather than chorea; moreover, "tetanoid" is not sufficiently distinctive. Anton proposed the term "dementia choreo-asthenica" to characterize his case, which is a case of congenital cerebral syphilis, but the title is for other reasons unsuitable. From the point of view of the most definite cases, to include "dementia" in the title gives that symptom undue prominence, even admitting that dementia is the correct term to employ. Objection, too, may be taken to the use of the epithet "asthenica." The asthenia of progressive lenticular degeneration is very different from that of neurasthenia or of Addison's disease.

It seems to me that "progressive lenticular degeneration" is a descriptive term which is brief, distinctive, based on pathological data, and at the same time non-committal, inasmuch as it entails no acceptance of a particular hypothesis as to the actual nature of the disease.

In view of the fact that the clinical symptoms are exclusively nervous, it is well to adopt a neurologically descriptive term. The essential fact of the hepatic cirrhosis may be mentioned in a sub-title. What I have done is to select what is by far the most striking pathological feature of the disease from the nervous standpoint and to utilize it for purposes of nomenclature, and, seeing that twenty years ago Ormerod and Homén noted exactly the same pathological changes in their cases, I think it will be conceded that the term is amply justified. In any case, it may remain till subsequent investigation finds a better.

Progressive lenticular degeneration may be defined as *a disease which occurs in young people, which is often familial but not congenital or hereditary; it is essentially and chiefly a disease of the extrapyramidal motor system, and is characterized by involuntary movements, usually of the nature of tremor, dysarthria, dysphagia, muscular weakness, spasticity, and contractures with progressive emaciation; with these may be associated emotionalism and certain symptoms of a mental nature. It is progressive, and, after a longer or shorter period, fatal. Pathologically it is characterized predominantly by bilateral degeneration of the lenticular nucleus, and in addition cirrhosis of the liver is constantly found, the latter morbid condition rarely, if ever, giving rise to symptoms during the life of the patient.*

(2) ETIOLOGY.

(1) *Age*.—Of those patients whose cases have been recorded as instances of progressive lenticular degeneration, the age of the youngest at the onset of the disease was 10 years; of the oldest 26. The average age, calculated from the series of twelve cases, is 15. In the more acute cases the disease made its appearance at a relatively earlier age than in the more chronic cases, but that it is essentially a disease of adolescence may be definitely concluded from the material before us.

(2) *Sex*.—Of the twelve cases seven were males and five females. In no one of the seven male cases was there any sign of physical infantilism, as far as can be determined from the published records, and from observation in my own cases. Of the five female cases, one of the patients, in whom the illness began at the age of 17, had never menstruated; in the other four the catamenia were established before the onset of the illness; thereafter in each case menstruation became irregular or ceased—an interesting fact, the significance of which is at present obscure.

(3) *Heredity*.—In no one of the series was there any definite history

of family nervous disease such as could be considered to be of any significance. Such details as a neurotic temperament in a parent, or consanguinity of parents, or weak-mindedness in an uncle, or alcoholism in a grandparent's old age, are not sufficiently precise to be of value. Nor was there a history of any special diathesis in the families concerned. Both similar and dissimilar heredity may be excluded in the case of progressive lenticular degeneration.

It is a curious fact, however, that of the twelve cases of the disease here analysed for statistical purposes, no fewer than eight are familial cases, and it is also curious that the families concerned are large.

Thus in family K. (Homén) there were eleven children and one miscarriage; the first, third, and fourth were affected and died of the disease.

In family M. (Gowers, completed by Wilson) there were fourteen children and several miscarriages; the first, fifth, and eighth were affected.

In family P. (Wilson) there were six children and no miscarriages; the first and second were affected.

Passing next to the families in which only one member was affected:—

In family T. (Wilson) there were nine children and no miscarriages; the eighth child was the patient.

In family To. (Wilson) there were three children and one miscarriage; the patient was the youngest child.

In family S. (Ormerod) there were four children, but it is not stated in what order they came; one child was affected; there were one or two miscarriages.

In family J. (Ormerod, Wilson) the patient was the only child, and there were no miscarriages.

It is possibly of some importance that in all the familial cases the eldest members were affected, and that, on the whole, the elder members suffered while the younger escaped.

The exact significance of the familial element, however, is debatable and difficult. All that may be concluded from the fact that the familial element does enter largely into the disease, is that there may be some special predisposition which cannot as yet be expressed in more definite terms.

(4) *Distribution*.—It is premature to generalize where there are as yet so few recorded instances of the affection. For documentary purposes, however, it may be noted that the K. family belonged to Finland, and lived in the country; the M. family have always lived in

the East End of London; most of the P. family were born in Italy, of English parents; the T. family is English, and from the country, as is the To. family.

(5) *Predisposing causes*.—The generalities to which the observer in search of predisposing factors is too often driven need not delay us. It may once and for all be stated that in my own series of cases there is no record nor any evidence of syphilis as an etiological factor; and this is true also of the other reported cases. Homén made a most exhaustive examination of the members of his K. family, but was unable to obtain any definite or unequivocal data in favour of the syphilitic hypothesis. It is true that with the Wassermann reaction to aid us opportunity should be taken to apply it in any future instances of the disease; personally, I was not in a position to take advantage of it in the only two of my cases which I had the chance to examine after the test was demonstrated to be of value.

There is no evidence that alcohol may be considered to be a predisposing cause. One of the M. family suffered from typhoid fever seven years before the onset of the disease, and another had an attack of the same fever about a year before the appearance of lenticular symptoms. Yet these facts cannot be held to be of any importance.

Reference will be made in another section to the interesting circumstances that two of my patients (Cases 1 and 4) had an attack of jaundice some years before the lenticular symptoms were noticed.

(6) *Exciting causes*.—These are uniformly absent. It is recorded with almost complete unanimity that the disease came on apparently without any exciting cause, and in an insidious manner. Speculation, therefore, is useless.

One thing is certain, however, in the midst of much that remains obscure. In my own series of cases the patients were of normal mental and physical development before the onset of the disease, and the same remark is made by other observers. If the disease is the expression of a degenerative tendency, an abiotrophic defect—which I do not think at all probable—then it is curious that it should single out individuals who seem endowed with mental and physical gifts that are well up to the average, and who in earlier years have, without exception, given promise of full development.

(3) SYMPTOMATOLOGY.

In progressive lenticular degeneration two clinical types may be distinguished, one acute or subacute, and the other chronic. Symptomato-

logically there is little difference between the two; the former is associated with some, it may be considerable, febrile disturbance, and the type of involuntary movements (which form a feature of every case of the disease) is not, perhaps, entirely identical with that of the more chronic cases.

Of the series of twelve cases, there are three which may be placed in the first category; in these the duration of the illness was four months, six months, and thirteen months respectively. In all, more particularly in the first, a high irregular temperature was present for a more or less lengthy period; emaciation was unusually rapid; the symptoms, speaking generally, were severe almost from the beginning, and the whole appearance of the patient suggested that he was seriously ill, as with a fever or any toxi-infective condition.

In the more chronic cases, of which there are nine, the patient's nutrition was well maintained, sometimes for a year or two; and he experienced a sense of well-being, for a long time at least, which was not belied by his looks.

In the main features of the disease, however, acute and chronic cases alike present a symptom-complex which is unmistakable.

If we scrutinize the record to discover the earliest clinical symptom, there is none that is constant in this respect, and in several instances more than one symptom is recorded as having resulted in attention being drawn to the patient. In some, notably the K. family, the earliest symptoms were mental rather than nervous; in most, they were nervous rather than mental. Whatever be the first symptom to make its appearance, it is not long ere the disease establishes itself by a series of symptoms which have developed with astonishing similarity in all.

Progressive lenticular degeneration is a motor disease *par excellence*; its most striking and characteristic symptoms are disturbances of motor function.

(a) *Involuntary movements: Tremor.*—Involuntary movements, and in particular tremor, form one of the outstanding features of the affection. In all my own cases tremor was one of the earliest symptoms, as it was one of the most marked; in Homén's family tremor was equally pronounced, as in at least two of the M. family—i.e., in nine of the twelve cases. In the other three it does not appear to have been quite so prominent, although present.

In the recorded cases the tremor has been a true tremor—i.e., it has consisted of a regular, rhythmical, alternating contraction of a given muscular group and its antagonists. The rate is variable, usually within

the limits of four to eight times a second. It is increased, as a rule, by excitement, or if attention is drawn to it, or by voluntary effort. Thus it was always brought out well in the finger-nose test. At other times it appears to be to a certain extent under the control of the will, for by the exercise of volition it can be somewhat diminished for a moment or two, though this is by no means a constant phenomenon. Thus, when one of my patients grasped my hand tightly, the tremor with which the effort was at first accompanied became less as the patient's grasp increased in power; but, on the other hand, under these circumstances, the tremor was likely to appear as an "overflow" in some other place—e.g., the leg. Sometimes, when the patient was left entirely to himself, a perfect riot of tremulous movements could be observed. In most cases the tremor is more evident peripherally than proximally—i.e., it chiefly affects the fingers and hands, or the toes and feet, and it also usually affects these segments first. Thus bad handwriting was frequently remarked as one of the early signs of the disease.

The range of the tremor is usually fine, at least at the outset; with volitional movement the excursions become wider, and as the disease progresses the tremor, according to the experience of all the observers, becomes worse in every way. In one of Homén's cases, however, with increasing contracture the tremor rather diminished, but came in "attacks," in which the whole of the body was involved. In the later stages of the affection it is usually incessant, and involves head and trunk as well as the limbs. In one of my own cases I was able, by relaxing every joint and putting the limb into a position of complete muscular rest, to make the tremor disappear, but whenever the support was removed and the patient innervated his limb again the tremor reappeared and increased with great rapidity up to its maximum. As far as one can gather, it usually or always disappears during sleep.

In some of the cases the tremor has been less noticeable than in others, and in one or two it is reported to have affected the lower extremities more than the upper. The tongue is often tremulous, but this is not the tremulous fibrillation of such a condition as general paralysis; on the contrary, while the tongue is being protruded there is tremor, but when it is fully protruded the latter disappears.

In one or two of the old cases, what caught the eye of the observer was not so much tremor as "tonic" or "clonic spasms." Thus in the case of S. M. (Gowers)—one of the acute cases—both arms presented slowly changing tonic spasm, greater in the left. Sometimes

the movements were quicker, and they were always increased by an attempt at volitional movement. In the legs there were similar involuntary spasmodic movements, in the trunk, and indeed in the musculature generally. There were occasionally paroxysmal exacerbations of such spasms, of a few minutes' duration. In the case of W. S. (Ormerod)—another of the acute cases—the muscles were in a state of tonic spasm, and on the slightest forcible movement clonic spasms were produced. In the case of Alfred K. (Homén)—a chronic case—it is specially noted that, in addition to the tremors, “during the last few weeks of life tonic and clonic cramp attacks occurred, of short duration, at the longest a minute.” On the other hand, in the case of C. M., the sister of S. M.—also an acute case—the involuntary movements were clearly of the nature of tremor, properly so-called.

It may be said, then, that in the chronic cases tremor was constantly present, and was pronounced and continuous; in two of the acute cases “tonic and clonic spasms” were met with; in the other acute case the movements were those of tremor.

(b) *Spasticity*.—Every one of the series of cases has been characterized by the presence of rigidity or spasticity, which has often reached an extreme degree. It has always been steadily progressive, and has resulted in the patient being reduced to a state of utter helplessness, unable to use his hands, unable to turn in bed, unable to recover his balance if that were disturbed. As a rule it has begun in the limbs, and in the cases which I have had opportunities of observing it has been more pronounced at the larger joints, possibly because here the muscles are naturally stronger and larger. The simplest way to convince oneself of the existence of this hypertonicity is to take one of the limbs, say the arm, and to impress on it passive movements of alternating flexion and extension at the elbow. Whichever be the movement made by the observer, he is always conscious of a considerable degree of resistance in the opposing muscles, so that quick passive to-and-fro movement of the forearm is an impossibility. The muscles always feel firm on palpation, and even when the limb is put into such a position as to relax any given muscle as far as possible, it can always be felt to be in a state of hypertonicity. Hence ensues an extraordinary degree of immobility in the advanced cases; the face is fixed, expressionless or smiling stiffly, and has consequently been noted as being “silly” or “fatuous.” The head and neck are equally fixed; even in the recumbent position the sternomastoids are not relaxed. The rigidity of the trunk

is such that maintenance of equilibrium becomes a matter of the greatest difficulty. As one of my patients was sitting on the edge of his bed he slowly fell backwards in a helpless fashion, with his legs in the air, quite unable to relax his hypertonic muscles or to use them to recover his balance.

As a rule the predominant hypertonic muscles are the flexors, though to this there are certain exceptions. In most instances the fingers and wrists are flexed, the elbows flexed, the arms adducted at the shoulders; the toes are curled under the feet, the feet turned in, the heels drawn up, the legs flexed at the knee and hip. In one of Gowers's cases, however, the limbs were extended at the knees, and at the elbows, and the arms were rotated inwards so that the palms looked back and outwards. It would appear that even in sleep the rigid condition of the musculature does not alter.

It is important to note, as will already have appeared, that in these cases we are dealing with a true hypertonicity of the muscles, involving both synergic and antergic muscles simultaneously. The rigidity is not due merely to inability to relax an antagonist, or to predominant flexor tonicity. As far as can be seen there is a generalized condition of increased tone in all the muscles indiscriminately, and the fact that this tonicity leads as a rule to the adoption of a flexor attitude is for the present immaterial. (*See also Chapter VI.*)

The solitary muscles of the body that do not appear to be implicated in this condition are the extrinsic ocular muscles. In my own cases their volitional movements were quick and free. Gowers, however, records that in the case of S. M. the movements of the eyes were normal, but at times the eyeballs rolled upwards. Ormerod remarks that in his patient the right eye "worked," but possibly this means that the muscles round the right eye were involved in the spasm which implicated the right side of the face. In the case of D. P. there were involuntary rolling movements of the eyes a few days before death—not a point of any special significance. Otherwise no voluntary muscle or group of muscles seems to be exempt. In my opinion the dysarthria and dysphagia, if not wholly, at least in great part, must be attributed to this rigidity. The open mouth of the patient provides a striking exemplification of his mental attitude in regard to this rigidity. If fig. 2, taken in 1886, is compared with fig. 21, taken in 1910, one cannot fail to note the indifference to the fact as expressed in the patient's face. He seems to be as unaware of the spasmodic depression of his inferior maxilla as he is indifferent to his tremor or oblivious of his sialorrhœa.

(c) *Contractures*.—It is but a step from rigidity to contracture. Contractures are as constant a feature of progressive lenticular degeneration as the involuntary movements. It is remarked of every patient that his or her limbs were grossly contracted towards the end. The contractures generally begin in the distal segments of the limbs, as exemplified in various figures which have been given in the clinical section. As the disease progresses so do the contractures, until they become extreme. It may be impossible to straighten the limbs out; two stages in the process may be noted, and two causes in its production. The first is the fixation of a limb in a particular position from hypertonicity of the musculature. This first stage is well illustrated by my Case 3. The patient looked as though his limbs were contracted up in the attitude of double hemiplegia or of paralysis agitans, but by dint of passive movement it was possible to extend them almost completely. This first stage is one of contracture-attitudes from hypertonicity, a purely nervous phenomenon. But secondly, as the result of the prolonged maintenance of fixed attitudes, myogenic contracture sets in, owing to permanent approximation of the origin and insertion of the muscles. This naturally shows itself most in those muscles which have caused the adoption of a given contracture-attitude: hence if this be one of flexion, the flexion contracture is accentuated, and the limb gets into a distorted condition from which no amount of passive movement can correct it. Thus we read that in one case the knees were right up on the patient's abdomen; in another the lower extremities were flexed at all joints; in a third the arms were permanently contracted at the finger-joints, wrists, and elbows; and so on.

It is apparent, of course, that "tonic and clonic spasms," spasticity or hypertonicity and contractures, are pathological conditions intimately allied to each other. Their pathogenesis will be discussed later, but at this point it is well to mass them together, as they may be present in varying degree in any given case of the disease, and it is desirable to realize that this possible variability, so far from confusing the diagnosis, is really to be expected from the nature of the affection.

(d) *Dysarthria; dysphagia*.—Dysarthria has been present in every one of the series of twelve cases, and in all it has advanced until it has resulted in more or less complete anarthria, the patients being unable to articulate intelligibly a single word or syllable. The dysarthria is characterized by the slurring element, without the staccato element, of the speech of disseminated sclerosis; the greatest difficulty is with certain consonants, and there is a frequent tendency to

abbreviate the ends of words. When at its worst the patient may still be able to phonate though articulation is impossible, hence unintelligible sounds may issue from the throat. Homén, Gowers and Ormerod have remarked on involuntary noises, or sounds, or moans, escaping from the patient. In my own cases this was not perhaps quite so marked.

The defect is in no wise comparable to that of general paralysis, and so far from there being facial overaction, as in the latter condition, the sounds escape from a mask-like, immobile face and mouth. Reference is made in a subsequent section to the variability in the dysarthria from time to time.

Dysphagia is as constant as dysarthria, and in a majority of the cases the two conditions have come on simultaneously.

(e) *Muscular weakness and emaciation*.—While progressive emaciation has marked the course of the disease both in the acute and the chronic cases, there is no record of local muscular atrophy. The wasting affects the musculature generally, and is associated, partly at least, with the contractures and the immobility of the limbs. Atrophy from disuse is a well-recognized condition. At the same time, some of the emaciation may very well be attributed to profound disturbance of metabolism, especially in the acuter cases, where, although the duration was shorter, the degree of wasting was, if anything, more severe.

In spite of the tremors, rigidity, and contractures, in the majority of the recorded cases a degree, and sometimes a considerable degree, of voluntary power has remained. Several of the previous writers have been struck by the apparent incongruity between the two facts, and the significance of the contrast will be discussed in the section on the pathological physiology of the disease. It is sufficient to note at present that in the early stages, at least, considerable muscular power may be retained, and voluntary movements may be of normal range, even though the patient gives the appearance of helplessness. In each of my own four cases the patients were still able to walk at a time when their appearance suggested complete spastic paralysis.

Muscular weakness, however, is undoubtedly one of the symptoms of progressive lenticular degeneration. Volitional movements may be good in range but they are usually resisted with comparative ease. This muscular weakness, also noted by previous observers, is not to be confused with clumsiness or awkwardness from hypertonicity or tremor. There is intrinsic muscular asthenia; the patient is incapable of any sustained effort; he cannot close his eyes tightly for any length of time, cannot keep his tongue protruded, cannot maintain his grasp. It may

be said, without risk of being misunderstood, that volitional innervation is defective, while involuntary innervation is exaggerated.

Admitting, however, the muscular weakness, one ought not to use the term "paralysis" to express it. The condition is one of muscular weakness without paralysis. "Paralysis," where motion is concerned, ought to be confined to diseases of the pyramidal system. In the case of progressive lenticular degeneration the motor symptoms are foremost, but except where contractures or rigidity forbid it the patient is able to move his limbs. Although the lower facial musculature looks immobile, the hypertonicity can sometimes be overcome sufficiently, and the patient will move his lips. He is not, therefore, "paralysed." There is no special term to indicate this specific motor helplessness resultant on disease of the extrapyramidal motor system.

(f) *Sensory*.—Compared with the motor, the sensory symptoms are minimal. On the subjective side, Homén observes that his patients suffered from occasional pains in the body and limbs, more especially the legs, and mainly at the beginning of the disease. Ormerod states that his patient had at one time paroxysms of pain, evidently associated with spasmodic contractions of the muscles, akin no doubt to painful cramps. The importance of these it is difficult to gauge; in any case the symptom is far from common and may be relegated to a secondary place. On examination no change in sensibility is discoverable. All of my four cases were carefully examined from the sensory standpoint, with a negative result. There are no sensory symptoms in pure lenticular disease.

(g) *Reflexes*.—In a pure case of the disease, such as my Case 3, there is no definite alteration in the tendon reflexes; they are active, but not exaggerated. Exaggeration of the reflexes is not a sign of lenticular degeneration in its uncomplicated form. It not infrequently happens that owing to the contractures they are elicited with difficulty. There is no ankle or other clonus. From the point of view of the cutaneous reflexes the only cases which have been examined with the help which knowledge of the significance of the plantar reflexes gives are my four personal cases. Of these, Case 1 had an extensor response on one side, but in view of the undermining of the internal capsule this is easily accounted for. Nevertheless, it must be remarked that in that case there is no descending degeneration in the pons, medulla, or cord. In Case 1, moreover, the abdominal reflexes were diminished on both sides. In Cases 2 and 3, which, clinically, be it observed, were just as severely affected as Case 1, the abdominal reflexes were normal—in

Case 2 they were readily obtained a few days before death—and there was a double flexor response. At the time when I last examined the patient whose case is No. 3, his condition was every whit as advanced as was that of Case 1, yet the state of the cutaneous and deep reflexes precluded the possibility of organic disease of the pyramidal tracts. In Case 4 the “boarding” of the abdominal muscles was no doubt the cause of the diminution or absence of the abdominal reflexes. A double flexor response was obtained. These facts are of primary importance from the standpoint of pathological physiology.

In every case of the series the organic reflexes are recorded as having being impaired towards the end; in fact, most of the patients have in the latest stages become “wet and dirty.” This is not to be taken as indicating local sphincter-defect such as one meets with in disease of the lower part of the cord (the spinal cords were throughout normal); on the other hand, I am not sure that it ought without further consideration to be attributed, as some would have it, to the mental deterioration of the patient, and to be interpreted as a sign of dementia. It seems to me that it may very well be due, in part at least, to increasing imperfection (of central origin) of voluntary control over the muscles concerned.

(h) *Mental symptoms.*—Of considerable interest are the psychical symptoms of progressive lenticular degeneration. It is a noteworthy fact that some form of mental change or impairment is specifically referred to in at least eight of the twelve cases; its importance, therefore, must not be underestimated. On the other hand, this mental impairment is highly variable both in degree and in kind, and therefore calls for some analysis.

Of Gowers's two patients one did not represent any definite mental symptoms; at least they are not referred to as such. The other is said to have been listless, lethargic, emotional, and easily excited to laughter. Ormerod's patient seemed “silly”; he became noisy and apparently idiotic; “his mental condition seemed to get worse, and he lay howling all day long.” Homén's three cases were all characterized by what he calls “dementia.” The symptoms he mentions may be thus generalized: listlessness, slowness of mental processes, “simple-mindedness,” failure of memory and of mental powers, emotionalism, stupid and idiotic facial expression, &c. My own first patient evinced a change in her disposition; at first she was restless and unable to settle to anything; she was easily provoked to laughter, her manners were childish, her mental powers to a certain extent diminished; but, on the other hand, her

memory remained good, at least for a long time after the disease was established, and on the receptive side little defect was observable. In Case 2 the earliest symptoms were that the patient became rather untidy in her dress, failed to obtain the same number of marks at school as formerly, later developed transient delusions, became emotional, and was easily provoked to laughter; "her younger sister had to be a mother to her," such was her childishness. In Case 3 the first symptoms were those of a moderately severe toxic or exhaustion psychosis, consisting in delusions, hallucinations of hearing, excitement, &c. They passed off entirely, never to return, but within a year the characteristic symptoms of progressive lenticular degeneration made their appearance, and in the case of this patient similar mental changes (though less in degree) to those already described in the case of his sister subsequently occurred. He was emotional, childish, facile; yet here also, while undoubtedly there was impairment of mental power, to some extent, on the afferent side no defect was to be seen. His memory and powers of recognition were for a long time unimpaired; his observation and perception were astonishingly quick. In the case of C. J., my Case 5, instead of remaining bright and intelligent, he became dull and stupid; he was very emotional, at one time laughing, at another crying; he was slow in answering questions, and in understanding everything that was said to him; but, on the other hand, he did everything correctly that he was asked to do. At the same time, it must be remembered that in my Case 4 no mental change is at present noticeable, and this has been the case in some of the earlier recorded instances of the disease.

In view of the frequency, then, with which some one or other psychical symptom is encountered in the disease, I am inclined to admit they form an important, though perhaps not an integral part of the clinical picture. An endeavour to specify the cardinal element or elements in them, or to classify them, is a matter of some difficulty. If the term "dementia" is to be employed to characterize them, it must not be forgotten that this dementia is decidedly limited. I carefully examined all of my patients from the point of view both of agnosia and of apraxia, but in no one of them were these symptoms present. Now it is just in the ordinary dementia of senility, of general paralysis, and to a less extent in dementia præcox, that these symptoms are most common, especially in the first of these. Hence the term "dementia" is not really appropriate. Disorientation in time and space is another of the common features of dementia, but in more than one

of my cases, if present at all, it was slight. The "dementia" of progressive lenticular degeneration cannot be likened to the steady mental involution of senile dementia, or of dementia paralytica, and it can be readily distinguished from dementia præcox.

The mental defects in the disease, when present, may occur in one or more than one of the following forms:—

(1) *Narrowing of the mental horizon*.—The patient does not seem to be able to add much to his store of mental images, and his capacity for retaining impressions is impaired; but within the limits of this constricted mental field his powers of perception and recognition are good. There are no delusions or hallucinations, as far as can be determined; and the mental condition does not deteriorate or degenerate *pari passu* with the physical condition of the patient. In Case 3 the patient, even *sub finem*, was perfectly cognizant of what was going on round him and was able to reply to questions by rational gestures. In one or two respects the mental condition is not unlike what may be seen in the early stages of Huntington's chorea.

(2) *Facility, docility, and childishness*.—The patient, especially as the disease is advancing, often becomes easily tickled, pleased, amused. Apparently he has no insight into his condition, for his cheerfulness is incompatible with knowledge of the seriousness of his illness. Some patients have not shown this euphoria, which, for that matter, is found probably only in chronic cases. The patient seems to be unable to deliberate or pass judgment on what is presented to him. Increase of emotionalism and of emotional reaction is not infrequently observed. Sometimes a condition resembling "rire spasmodique" is met with, never "pleurer spasmodique." This involuntary laughter is no doubt associated with the disease of the basal ganglia. (See below, p. 477.)

It may, however, be again remarked that some cases do not show much or any obvious mental change, while others present mental symptoms that are unique as far as each individual case is concerned.

(i) *Symptoms referable to other systems*.—The only system to which reference need be made is the alimentary. Homén's patients suffered from occasional sickness, one of them from frequent vomiting. All had loss of appetite as one of the initial symptoms. Neither Gowers's nor Ormerod's patients showed any gastro-intestinal symptoms, if we except what seems to have amounted to bulimia in the latter case, at one stage of the illness. No one of my patients presented any symptoms referable to the alimentary system, except Case 1 *sub finem*. With the exception of the case of C. J., No. 5 in my series, not one of the

patients was found during life to have definite symptoms or signs of disease of the liver—i.e., while lenticular symptoms were present. In Case 1 of my series it may be remembered that an attack of jaundice occurred some years before the onset of the lenticular disease, and this patient suffered from severe hæmatemesis just before death; similarly, in Case 4 there was a history of an attack of jaundice some years before the onset of the lenticular symptoms.

It is a remarkable fact that in ten cases advanced hepatic cirrhosis has been found on *post-mortem* examination when symptoms of it during life have been conspicuously absent.

(j) *Negative signs.*—If negative signs are ever of any value certain of them may be tabulated here.

In progressive lenticular degeneration: The optic discs are normal; the pupillary reactions are normal (in only one case were the pupils said to be sluggish to light); there is no nystagmus; the palate moves on phonation and reflexly; there is no fibrillation or localized amyotrophy; there are no cerebellar symptoms; there is no impairment of sensibility; the reflexes are not those of pyramidal disease.

There are certain general features in the symptomatology of the disease to which attention must be directed, as they help to an understanding of the condition. These are, briefly, the pronounced variability in the symptoms from time to time, and the resemblance which some of them may present at a certain stage to what is called "functional" disease. A discussion on these points will be raised in a subsequent section (p. 459).

(4) PATHOLOGY.

In analysing and synthetizing the pathology of ten cases of progressive lenticular degeneration, the first point to draw attention to is that in three cases the examination of the central nervous system proved negative—viz., S. M. and C. M. (Gowers) and C. J. (Ormerod, Wilson). On the other hand, in the case of W. S. (Ormerod), Homén's three cases, and three of my own cases, symmetrical bilateral lenticular degeneration was found—i.e., in seven out of ten cases, a sufficiently large proportion to justify one in expressing the opinion that a minute microscopical examination of the corpus striatum in the other three, the negative, cases, might have revealed some pathological changes. In the case of S. J., only a macroscopical examination of the brain was made, apparently, and it was negative. In the cases of

S. M. and C. M. "pieces of the cortex, cord, nerves and muscles," were examined microscopically, with a negative result. There is no reference to a microscopical investigation of the basal ganglia. Now in view of the fact that in these very structures—viz., cortex, cord, nerves and muscles—examined in each of my three personal cases with modern histological methods, no definite changes of any significance could be detected, it is little wonder that the examination of twenty-two years ago was negative. The point is that in the acute cases it is quite possible the only lenticular change may be a microscopical one, if indeed it is to be seen at all. We have the evidence of Ormerod's case (one of the acute cases) to show that pathological changes in the lenticular nucleus may be recognized after a few months; on the other hand, in the case of C. M. the duration was thirteen months, and a priori, had any naked-eye lenticular change been present it was sure to have been detected. An argument by analogy from two of my series—viz., Case 1 and Case 3—may be stated in this connexion. In the former the pathological changes were much more advanced than in the latter, yet clinically no such difference in degree obtained. Hence, we must not judge of the severity of the clinical symptoms by the degree of pathological and structural change found at the autopsy. Accordingly, it may fairly be held in the case of C. M. that the function of the corpus striatum may have been dynamically disturbed without much structural change being recognizable.

In the seven cases with positive findings in the central nervous system the appearances are so similar that they afford striking proof of the selective action of some morbid agent. In all, with the exception of my Case 2, where the examination was incomplete, but where the assumption that the case was identical with the others is abundantly justifiable, there is bilateral symmetrical degeneration of the putamen, and of the globus pallidus to a less extent. Various degrees of this degeneration are found, from discoloration and sponginess of the nucleus, through shrinkage and atrophy to complete disintegration and excavation of the ganglion. Neighbouring structures are involved to a much less extent; the caudate is often rather shrunken, but never disintegrated as is the lenticular nucleus. The optic thalamus is practically always normal, except in so far as loss of striothalamic fibres may affect its lateral part ("zone grillagée" and lamina medullaris externa); and in pure cases the internal capsule is intact from end to end. Sometimes the external capsule is degenerated, mainly in its middle or posterior third; the claustrum is usually normal, and the convolutions of the island of

Reil normal, though sometimes the latter show diminution of cortical fibres, and a certain slight loss of substance. Apart from the degeneration in the lenticular nucleus, the changes in the brain are insignificant. There is no evidence of established meningitis; sometimes slight leptomeningeal thickening is found, patchily distributed. The cerebral cortex offers little definite alteration; Homén found the frontal cortex possibly somewhat thinned, with slight diminution of myelinated fibres, but there is no wholesale chromatolysis (by Nissl's method) in any of the modern cases; on the contrary, and more particularly in the motor area of the precentral convolution, the cortex is practically normal. The Betz-cells are well up to normal numbers and stain well. There is no sign in the modern cases of any small-cell infiltration anywhere; Homén found slight traces of this in his cases, but remarks that it is nothing like so pronounced as is met with in dementia paralytica; Ormerod found small-cell infiltrations in the lenticular nucleus in his acute case.

The microscopic changes in the lenticular nucleus in the chronic cases are not, however, accompanied by small-cell infiltration. They consist of glial overgrowth, which afterwards disintegrates and breaks down; there is often an immense increase in glial nuclei; the nerve-fibres and nerve-cells of the normal nucleus disappear; "Körnchenzellen" and macrophages are frequently present in numbers. Even when the cavity formation is extreme there are no signs of obliterative endarteritis in the blood-vessels, the perforating lenticulo-striate vessels and their branches; on the contrary they are, if anything, thinned, and are sometimes hyaline. Very occasionally their adventitia seems thickened; the intima never. Round the vessels gaping spaces make their appearance, possibly from shrinkage of the nervous tissues, hence the nucleus presents a finely worm-eaten appearance; this is a stage previous to cavitation. In Homén's cases more definite disease of the blood-vessels was found than in my cases. He notes that they were irregularly sclerotic—i.e., had patches of degeneration in their walls, with small collections of granular material between the coats of the vessels; sometimes the granular material bulged into the lumen of the vessel. Sometimes they were the seat of hyaline degeneration. The intima, nevertheless, is not stated to have been pathologically altered. Changes of this kind he found in all his cases, nor were they confined to the arteries of the basal ganglia.

The pons, medulla, and cord are uniformly negative from the pathological point of view, any changes which they may present being of secondary importance. This is true also of the nerves and muscles.

In the modern cases certain degenerations consecutive to the main lenticular disease can be traced. These are, in advanced cases,

degeneration of the ansa lenticularis, relative atrophy of the corpus Luysii, partial degeneration of the lenticular bundle of Forel and of the strio-Luysian fibres, and degeneration of striothalamic fibres.

Two other organs are commonly affected in this disease—viz., the liver and the spleen. The liver is always cirrhotic, from hepatitis, and I do not think a diagnosis of progressive lenticular degeneration can be made in any case in which the liver is not thus affected; in other words, I consider it is essential. In several of the cases the spleen is reported as having been enlarged, but without any other change. The exact significance of this is at present obscure.

The cirrhosis of the liver is always advanced, and strikingly apparent. The organ is usually rather smaller than normal, but not constantly so. It is firm, hard, tends to preserve its shape, and presents the appearance of rounded nodules of liver-tissue clustered together, of the size of hazelnuts or larger, separated by depressed cirrhotic bands. The organ is never bile-stained, but is often rather lighter in colour than usual. Microscopically are found normal areas, necrosed areas, fattily degenerated areas, and actively regenerating areas, scattered irregularly through the organ. The type of cirrhosis is mixed—i.e., it is mostly multilobular, in some places monolobular, and occasionally there are indications of intralobular cirrhosis. So-called hypertrophying bile-ducts are often seen in the new connective tissue formation. Finally, this cirrhotic new formation is often very narrow, and in some places is very cellular, in others more fibrous.¹ In certain of my own cases the pituitary and suprarenal were apparently normal, as was the kidney; the thyroid showed regressive and proliferative changes.

(5) DIAGNOSIS.

To anyone familiar with the disease its symptomatology and course must appear so characteristic that he may well think it a *morbis sui generis*. It offers so many features that are almost unique, that it is difficult to see how confusion might arise. The acute cases, for instance, which run a course of a few months, are in my opinion really unique. They do not offer analogies with any other nervous condition with which I am acquainted.

Of the affections with which progressive lenticular degeneration

¹ Several questions in reference to the occurrence of hepatitis in young people, and in families, and in reference to the exact nature of the cirrhosis in progressive lenticular degeneration, will be discussed in a separate communication.

might conceivably be confused, disseminated sclerosis may first of all be mentioned. Yet the resemblance is but superficial. In the former there are no nystagmus, optic atrophy, amblyopia, paræsthesiæ, objective changes in sensibility, absence of the abdominal reflexes, extensor responses and ankle-clonus. The dysarthria in the two affections is not identical; the rigidity of disseminated sclerosis is rarely, if ever, so universal or complete as in the other; contractures do not form so essential a feature of the symptomatology. The course of disseminated sclerosis is much more variable and very often longer in duration. It is only in the early stages that confusion is possible, when there is as yet absence of organic signs, so called; a patient who suffers from intention-tremor and slight dysarthria is certainly difficult to place when other signs fail.

The differential diagnosis from bulbar palsy should present no difficulty, and need not be enlarged upon. Pseudobulbar paralysis, however, may be more difficult to distinguish. Pseudobulbar paralysis is a disease of the pyramidal tracts, of that section of them which goes from the lower part of the motor area via the genu of the internal capsule ("faisceau geniculé") to pontine and bulbar motor nuclei. The result of bilateral (much more rarely unilateral) involvement of these fibres is the production of dysarthria, dysphagia, inability to protrude the tongue, paralysis of the palate, paralysis of the lower part of the face, sialorrhœa, often involuntary laughter, &c. Such a clinical picture of course in some ways resembles, so far as it goes, that of progressive lenticular degeneration. There is a further complication. The fibres from the operculum, forming the "faisceau geniculé," run partly in the external capsule, and skirt the lenticular nucleus (without, however, actually passing through it except to a very slight extent at its upper and anterior extremity) on their way to the genu of the internal capsule. It may therefore be questioned to what extent a large lesion of the lenticular nucleus, especially if the external capsule be to any extent implicated, must not of necessity involve some of the geniculate fibres, and, if it is bilateral, thus occasion a degree of pseudobulbar palsy, apart altogether from the true lenticular symptoms; the latter, coming on top of the former, may not easily be distinguished, if at all. I believe that in one or two of my cases (especially of course Case 1), the geniculate fibres were involved to some extent, apart from the lenticular disease. In Case 3, however, the genu is apparently intact on both sides, and if the geniculate fibres are at all affected directly, this can only be through some involvement of the external capsule.

In typical pseudobulbar cases the palate and tongue are. In progressive lenticular degeneration they are only apparently the palate moves on phonation, and the tongue can be pressed slowly. In other words, in pure cases of the disease the dysphagia, &c., are the result of the rigidity of the motor muscles concerned, comparable to the rigidity of the general skeleton. As the disease progresses, should the geniculate fibers be involved, the clinical picture will change, though the process is easy to detect, to that of true pseudobulbar palsy. As a rule the latter condition presents symptoms of double hemiplegia; a condition of the reflexes will serve to distinguish the hemiplegia from the "paralysis" of progressive lenticular degeneration.

Paralysis agitans is a disease in several ways closely related to progressive lenticular degeneration. The age of onset in the latter, however, is by itself almost sufficient for differential diagnosis. The latter is a disease of youth. Paralysis agitans is very chronic, and speaking generally the attitudes of that disease are specific, in their own way, as those of the other, from which they differ considerably. The question of the analogies between the two is discussed in a subsequent paragraph (p. 479).

Juvenile general paralysis may be mentioned, only to be distinguished.

(6) DURATION AND PROGNOSIS.

The experience of all who have had opportunities of following the course of the disease is that it is invariably fatal. It may be said, however, that in most of the cases the diagnosis was not made until the patient reached the *post-mortem* table, and it is conceivable that some of the cases, which have not, however, been recognized, might have recovered; nevertheless, I do not think this probable. Though the affection is always steadily downwards; remissions are so scant as scarcely to be worth the name. The outlook, once a diagnosis is made, is always serious and may at any time become grave. The duration of the three acute cases was four, six and thirteen years respectively. The shortest of the more chronic cases lasted half a year; the longest case on record is one of Homén's, which lasted on for seven years. The average duration of the first three cases is three and a half years. The average of eight chronic cases is almost exactly four years.

KNOWN CASES OF PROGRESSIVE LENTICULAR DEGENERATION

SYMPTOMATOLOGY				
	Sensory	Reflexes	Mental	Brain
phagia, emaciation, "work"	Nil	Not known	Nil	
phagia, emaciation and "	"	Plantars "slight," abdominals absent, knee-jerks present	"	Nothing definite
remors, contraction	"	Knee-jerks present, later absent (? from spasm)	Emotional	"
phagia, emaciation, "clo-	Pains in limbs	Knee-jerks active	Emotional, "idiotic," "howls vehemently"	Bilateral scapular
muscular contraction, asmodic emaciation	Nil	Knee-jerks active, abdominals present, plantars "brisk"	Emotional, dull, stupid	Nothing definite
weakness, phagia, rhythmic, "tonic amps"	Pains in limbs	Cutaneous reflexes "weak," tendon reflexes difficult to test	Dull, listless, "simple"	Bilateral softening, thickening of meninges, slight frontal atrophy
weakness, tremor, dysphagia	Pains in limbs	Tendon could not be tested, cutaneous "weak"	"General appearance suggested dementia"	Bilateral cavitation, frontal atrophy, convulsions
weakness, arthralgia, emaciation	Pains in limbs	Not mentioned	Apathetic	Bilateral softening, regular thinning of membrane
phagia, contraction, emaciation, athymia	Nil	Abdominals dim., knee-jerks present, plantars at first flexor, later extensor L.	Emotional	Bilateral cavitation, capsule slightly thickened
phagia, contraction, emaciation, athymia	"	Abdominals present, plantars flexor	Emotional, facile, transient toxic psychosis symptoms	Right lenticular degeneration, also lateral capsule
phagia, contraction, emaciation, athymia	"	Abdominals present, plantars flexor	Emotional, facile	Bilateral degeneration, lateral capsule slightly thickened
phagia, rigidity, contraction, tremors	"	Abdominals not obtained (? from rigidity), plantars flexor	Nil	
phagia, tremors, muscular	Nil	Not mentioned	Apathetic	"Membrane and sub-brain soft from acute

analysed. For description of case, see footnote p. 319.

PATHOLOGY			Number
Liver	Spleen	Other findings	
<i>10 post-mortem</i>			1
Cirrhosis	Not mentioned	..	2
"	"	..	3
"	"	..	4
"	Large, firm, congested	..	5
"	Normal	Slight sclerotic or hyaline changes in smaller cerebral blood-vessels	6
"	Enlarged, firm	Small localized granular and hyaline changes in cerebral blood-vessels	7
"	Normal	A few circumscribed endarteritic changes in certain cerebral blood-vessels	8
"	Firm, congested	Slight changes in thyroid	9
"	Enlarged	..	10
"	Enlarged, firm	Changes in thyroid: pituitary and suprarenal normal	11
Still living			12
Cirrhosis	Enlarged	..	13

TABLE SUMMARIZING ALL THE

Number	Initials	Author	Year when case came under observation	Sex	Familial or otherwise	Age at onset	Duration of illness	Result and age	Motor signs
1	Sl. M.	Gowers, Wilson	1879	M.	Familial	10 yrs.	4 years	Death at 14	Anarthria, dy contractures, tion, "limb stantly on th
2	Sy. M.	Gowers	1886	M.	"	10 "	4 months	" 10	Anarthria, dy contractures, tion, "ton clonic spasm
3	C. M.	Gowers	1888	F.	"	15 "	15 "	" 16	Dysarthria, spasmodic tures, emaci
4	W. S.	Ormerod	1889	M.	—	10 "	6 "	" 10	Anarthria, dy contractures, tion, rigidity nic spasms"
5	C. J.	Ormerod, Wilson	1889	M.	—	11 "	2 years	" 19	Dysarthria, weakness, tures, rhythmic mors and sp contractions tion
6	Ad. K.	Homén	1889	M.	Familial	20 "	3 "	" 23	Stiffness, w anarthria, dy contractures mical tremor and clonic c
7	W. K.	Homén	1888	M.	"	12 "	7 "	" 19	Rigidity, w contractures mors, anarthria phagia, emaci
8	Aa. K.	Homén	1888	F.	"	20 "	6 "	" 26	Stiffness, w tremors, anarthria, dyphagia, tion
9	S. T.	Wilson	1906	F.	—	26 "	4½ "	" 30	Anarthria, dy rigidity, tures, weakn ciation, rhythmic tremors
10	D. P.	Wilson	1906	F.	Familial	17 "	2½ "	" 19	Anarthria, dy rigidity, tures, weakn ciation, rhythmic tremors
11	E. P.	Wilson	1907	M.	"	19 "	3 "	" 22	Anarthria, dy rigidity, tures, weakn ciation, rhythmic tremors
12	M. To.	Wilson	1911	F.	—	18 "	Still living, aged 20 years		Anarthria, dy rigidity, cont weakness, em rhythmic t
19*	C. Z.	Frerichs	1854	M.	—	9 yrs.	About 1½ years (?)	Death at 10	Dysarthria, dy weakness, slowness of movement

* Not included in the ca

(7) TREATMENT.

What can be said of the treatment of the disease? Its nature must be discovered before treatment can be lifted from the empirical to the rational level. All that can be done by those who have had charge of cases is treatment of an essentially symptomatic and palliative kind. In my Case 4, at present under observation, I am trying the effect of urotropine, administered over a long period of time.

CHAPTER V.—NATURE AND PATHOGENESIS OF THE DISEASE.

WHEN we leave the realm of facts to face the problem of the nature and pathogenesis of progressive lenticular degeneration, difficulties begin. The first impression of the disease is that it is so different, apparently, from most familiar morbid types, as to constitute a class by itself, and that there is no other affection with which to compare it. It is true that this disease is, I believe, the first definitely established morbid entity whose most striking characteristic is a specific association between disease of one of the viscera and disease of a particular part of the grey matter of the central nervous system—viz., the lenticular nucleus. The mystery, however, is perhaps not so impenetrable as may at first appear. There are certain symptoms of the disease which furnish a clue to its nature, and further, there are certain analogies to be drawn from other diseases, as will shortly be seen, which will aid materially in the attempt to explain its pathogenesis.

First of all, the opinions of the older writers may be quoted. To the clinical acumen of Gowers, Ormerod, and Homén, the student of the disease is greatly indebted, for each, recognizing he was dealing with a disease *sui generis*, examined his cases and published the record with a fulness of detail which leaves nothing to be desired. I count myself fortunate to have had access to the original notes of some of these cases, for a link is thus formed between the old and the new which enhances the scientific value of each.

Gowers, the observer of the earliest cases, writes as follows [4] :—

“In the two cases I have recorded no symptom of inherited syphilis was present. The probability of inherited syphilis as the cause of the malady of the nervous system rests entirely on the significance of the hepatic cirrhosis, whether or not syphilis is the only cause of the juvenile non-alcoholic form. Even the assumption of this causation leaves the direct pathology as mysterious as before. It is inconceivable, in the first case, and most improbable in the second, that any coarse

morbid process could have existed and have escaped the careful examination to which the nerve-centres were subjected. The facts seem compatible only with a blood state as the cause of the symptoms.

"But if a blood state caused the symptoms, the question arises: Were this and the cirrhosis of the liver the common effects of one cause, or can the blood state have been the effect of the hepatic disease? Anomalous as the last assumption may seem, it cannot be hastily dismissed. In connexion with the difference in the character of the symptoms, there is also the association of the higher fever in the second case with a greater degree of disease of the liver. Toxic blood states may be complex in causation; one derangement of the chemical processes of the system may induce others, the effects of which co-operate with the first."

Ormerod [7] makes the following remarks, in addition to what has been already quoted from his paper:—

"The German cases which we shall quote presently make it probable that the softening in the neighbourhood of the lenticular nuclei had some essential connexion with the disease; but it will hardly explain the whole course of symptoms. . . . Professor Homén apparently would explain the whole of these morbid appearances as being due to inherited syphilis, though there was no clinical evidence of this. Upon the intimate nature of the disease, however, an opinion can hardly be given till more observations have been made. . . . Whether it is right to put the cirrhosis of the liver in as prominent a place as I have done in the heading of this paper, must be judged by the comparison of other similar cases, but I think it can hardly be counted as a coincidence."

Homén [6], in the course of his remarks on the pathogenesis of the disease, says that everything points to the vessel-degeneration as the primary lesion. As there was no sign of acquired syphilis in his patients, and indeed, apparently, no possibility of its having been acquired, Homén is driven to the conclusion that the syphilis, which he postulates for the vessel-degeneration, must be congenital or hereditary. Yet he is doubtful himself about his own contention. In cirrhosis of the hereditary syphilitic type the pathological picture is different from that of his cases, and clinically the presence of ascites is practically constant, whereas it was absent in all of them. He concludes in the following guarded terms:—

"If we consider, finally, all the pros and cons, we must conclude, taking all the circumstances into account, that even though positive evidence is wanting, yet in all probability we are dealing with an unusually

late manifestation of hereditary syphilis. This is more than a mere predisposition, and since the probability is that at the time of the begetting of the children the syphilis of the parents—"had disappeared, or almost disappeared, it follows that its effect on the offspring is delayed, and not characteristic; it appears more as a special form of disease to which the syphilis bears only a remote relation."

Apparently Homén feels that the disease ought to be considered a parasymphilitic condition, although he does not actually use the expression, for he refers both to tabes and general paralysis in this connexion—viz., that of the remote action of syphilis.

These speculations of the older writers on the subject serve to emphasize the obscurity that surrounds the disease. To-day, however, there are no fewer than twelve cases (ten of which came to autopsy) to which we may turn for an independent consideration of the clinical and pathological data they furnish, and we are in a better position to appreciate the importance of certain factors. There is sufficient material at our disposal to warrant the assertion that where so definite a morbid entity is concerned some conception of the nature and pathogenesis of the disease must be forthcoming. Modern tests and methods of examination, moreover, provide considerable assistance.

(1) IT SEEMS CERTAIN THAT THE DISEASE IS NOT DUE TO A
CONGENITAL OR ABIOTROPHIC DEFECT.

Homén himself has remarked on the normal physical growth and mental development of his patients, previous to the onset of the disease. I have the evidence of the mother of the M. family, that this is true, also, of the three members of her family who eventually succumbed to it. Neither in Ormerod's nor in my own cases was any stigma of degeneration discoverable, or any mental or physical defect noted as rendering the children in any way different from their fellows. On the contrary, they all promised exceedingly well. Four of the five female cases had normally established catamenia previous to the onset of the disease. The evidence against the suggestion appears so conclusive that it is superfluous to elaborate the point.

(2) THE PRESUMPTION THEREFORE IS STRONG THAT THE DISEASE IS
ACQUIRED.

Although a majority of the cases are familial, the fact ought not to be overlooked that in the T. family the sole member affected was

the eighth child, whose case turned out to be, nevertheless, one of the most typical of all (my Case 1). Similarly, in the To. family only one member was affected. There is therefore nothing *essentially* familial about the disease, in spite of the frequent occurrence of familial cases. Nor has any congenital or hereditary instance of the disease been reported. Further, the acuteness of the malady (in some cases) is unlike any congenital or hereditary affection, and the fact that it occurs always in young people brings it into line with more than one well-known toxi-infective condition which has a predilection for youth. These points are in favour of the disease being one that is acquired. The only difficulty, in regard to the familial element, is that sometimes members of a family are affected at long intervals of time one from the other. Thus in my Case 5 the illness began some seven years before it appeared in the patient's brother and sister; they were 3 and 6 years old respectively at the time. Again, five years elapsed between the appearance of the disease in Homén's case W. K., and his case A. K. There is no simultaneous affection of several members of a family, as in such toxi-infective conditions as poliomyelitis, so that it may be debated whether there is not an inherited tendency to the disease, as it may appear at long intervals in the same family. In this connexion it might be instructive to attempt to discover whether in these familial cases the patients who suffered were placed in circumstances different from their brothers or sisters, or were in any way exposed to risks which the others did not run. In my own cases I have not been able to glean any information that is germane to this subject. The matter must be left for the present, until subsequent investigation throws more light on the exact nature of the morbid agent.

(3) THERE IS EVIDENCE TO SHOW THAT THE DISEASE IS TOXIC IN ORIGIN, BUT NONE TO SUGGEST THAT THIS TOXIN IS SYPHILITIC.

The arguments on which this statement is based are of two sorts: those which may be advanced from a study of the acute cases, and those which analysis of certain features of my own cases leads me to offer.

(a) All the acute cases are more than twenty years old, and we must be content with a scrutiny of the old records.

Now, in Gowers's and Ormerod's cases, the duration of which was six, thirteen and four months respectively, it is clear we are dealing with an acute illness, steadily and rapidly progressive, associated with high, irregular fever, and with profound disturbances of general meta-

bolism; the symptoms vary from week to week, yet no definite improvement is recorded; from being plump, healthy, intelligent children the patients are speedily reduced mentally almost to the level of "imbecility," and physically to "skin and bone," an expression which cannot be said to be exaggerated—and all within the space of a few months. No morbid process, I submit, can be conceived so widespread in its action and so fatal in its incidence as this, other than a toxic or toxi-infective process.

(b) Certain facts in my own cases suggest a toxic origin for the disease.

The clinical history of E. P. (Case 3) is important in this respect. His illness began rather suddenly and unexpectedly, with certain mental symptoms, viz., motor excitement, disorientation, auditory hallucinations, &c.—symptoms which are indicative of a toxic psychosis. In other words, they are the symptoms commonly appearing when the cerebral cortex is thrown out of gear as the result of toxic action, whatever that toxin be and whatever its origin. From this typical toxic psychosis the patient made a good recovery, yet within a few months of his discharge from the hospital the physical symptoms of progressive lenticular degeneration made their appearance. This fact is at least suggestive of the continuance of the action of some toxin on the nervous system.

Again, the transient mental symptoms from which his sister suffered in the early part of her illness, as distinct from the general mental deterioration—such as it is—which some patients with progressive lenticular degeneration show, suggest an intoxication of some sort. I do not think the argument is invalidated by the objection that in neither case were these symptoms persistent. Considering the variability of action of toxins, and the fact that a part of the brain other than the cortex is more profoundly affected, so that other nervous symptoms are more in the clinical picture, it is not remarkable that this should be so.

(c) The variability of many of the symptoms from time to time suggests a "functional" or "nutritional" rather than a structural change.

Gowers, Ormerod, Homén, and myself have in turn been struck by the odd way in which the patients, seemingly so inarticulate, have occasionally been able to utter words or phrases with comparative ease and distinctness. Similarly, notwithstanding their appearance of helplessness, in the early stages of the disease their voluntary movements and their muscular control and power have so varied from time to time that the suspicion has crossed the mind of more than one

observer that the condition was "functional." This being so, and in the absence of so-called "organic" signs, it is natural to suppose that some morbid agent is at work producing varying disturbances of function while structural change is as yet slight, and no agent is more likely to produce that form of disturbance than some form of toxin, autogenous or otherwise.

As for the question of this toxin being syphilitic, the whole weight of the pathological evidence in my cases is against that hypothesis, even if we ignore the fact that clinically there is no more reason why syphilis should be proposed as a possible explanation of the disease than, say, malaria. There is no single pathological lesion in my cases, of vessels or meninges or viscera, which resembles what is found in syphilitic disease of these structures. In none of the old or the recent cases is the liver condition identical with, or suggestive of, a congenital syphilitic liver. Further, the pathological evidence of Homén's cases cannot, in my opinion, be taken to support a syphilitic hypothesis. The remarks already quoted from Homén show his own theory to be that the disease is parasyphilitic, *faute de mieux*. Finally, although acute syphilitic meningitis is a recognized clinical and pathological entity, it is nosologically irrational to conceive of syphilis hereditaria tarda causing an acute and rapidly fatal illness—in a few months—after years of normal, healthy, mental and physical development.

(4) IT IS POSSIBLE THIS TOXIN MAY BE ELABORATED IN THE LIVER.

Cirrhosis of the liver is an absolutely constant feature of the disease, and the opinion therefore is not unwarranted that it must be integrally associated with the pathogenesis of the condition, the more so because it is the sole visceral change which is always found *post-mortem*. The question remains: Is the cirrhosis primary, and the lenticular degeneration secondary, or are both the effect of the action of some morbid agent? We have already seen reason to believe that the disease is of toxic origin. The problem, then, may be stated in another way: Is a toxin liberated or elaborated in the liver which has a double action, on the liver itself and on certain nervous tissues? Or is it produced elsewhere, and has it a simultaneous incidence on the liver, producing cirrhosis, and on the lenticular nucleus, causing the latter to degenerate? Or does some morbid process act on the liver, which is thus made to produce a poison that affects the corpus striatum? How does the presumed toxin act, and what is its nature?

It is obvious, of course, that such questions are more easily posed than answered. One or two points, however, may be alluded to.

While all previous writers on the subject have remarked on the absence of hepatic symptoms during life—in this connexion the loss of appetite and occasional vomiting of Homén's patients cannot be regarded as specific—there are three cases in the series in which certain liver symptoms were present at one time or another, and it is to these that attention must now be drawn.

At the age of 21, S. T., my Case 1, had an attack of jaundice of five weeks' duration, and for several years thereafter she showed at intervals definite signs of persisting liver disease in the form more particularly of œdema of the legs and feet. Four years after this attack, and at a time when the liver disease could not have been long in abeyance, the earliest symptoms of progressive lenticular degeneration made their appearance, in the shape of bilateral tremor. Such a sequence of events is very suggestive, although I admit, as far as the series goes, it is all but unique. It may be taken to show that where liver symptoms are present at all they antedate the lenticular symptoms. Similarly, M. To., my Case 4, had a definite attack of jaundice, of about three weeks' duration, some three and a half years before the onset of the lenticular symptoms. In her case the jaundice cleared up without leaving any "reminder" of hepatic mischief, in the shape of œdema or otherwise. Nevertheless the association is important, and the same deduction may be made from this case as in Case 1—viz., that if liver symptoms occur they precede the nervous symptoms.

C. J., my Case 5, had unmistakable liver symptoms during life in the form of ascites and œdema, and in this respect the case is unique; none of the others has presented the combination of liver and of lenticular symptoms at one and the same time. From the clinical record, it would appear that the two ran a course *pari passu*. What importance to attach to these facts it is difficult to determine. Cases both more acute and more chronic than this one have not shown any liver symptoms at all. There may have been some pathological complication which produced them in the case of C. J.

If we suppose the condition to be of toxic origin, we have to account for the continued action of the morbid agent, as it is unlikely that once lenticular degeneration commences it must inevitably proceed without further aggravation. Now, when it is remembered that the disease of the liver—a hepatitis with resultant cirrhosis—is a universal feature, that it is always advanced, even in the

acute cases, and that no other viscus shows a constant change, it is natural to suggest that this disease has much to do with the continuance of action of the toxin. Further, the microscopical evidence furnished by examination of the liver proves that the changes in it are always active, for necrosis and regeneration proceed side by side. This may, I think, be taken to suggest that the morbid process is never in abeyance, as far as the liver is concerned, and that fresh areas of that organ are attacked while others recuperate. On the other hand, as Homén's and my own cases conclusively demonstrate, the longer the duration of the disease the greater the disintegration of the lenticular nucleus. Hence we are justified in advancing the hypothesis that the disease of the liver is in some way the cause of the lenticular disease.

While perhaps it may be a little difficult to conceive of toxic action as prolonged as one or two of the cases are presumed to show, it must not be forgotten that between the acute and the chronic cases there is no noteworthy distinction, as far as duration goes. The exact duration of the series of cases, in order of length, is as follows: 4 months, 6 months, 13 months, 2 years, $2\frac{1}{2}$ years, 3 years (two), 4 years, $4\frac{1}{2}$ years, 6 years, 7 years. There is no abrupt interval between the acute and the chronic types. This fact by itself is in accord with the hypothesis here offered.

(5) THE TOXIN HAS A SPECIFIC ACTION ON THE LENTICULAR NUCLEUS.

A toxic condition usually suggests a generalized condition, but many toxins have a specific action, instances of which readily suggest themselves. In progressive lenticular degeneration the action of the toxin is both general and local. Among the effects of the former process are the disturbances of metabolism, more particularly in the acute cases, the mental signs of toxæmia, and so on. The local effects of the toxin are seen in the degeneration of the lenticular nucleus on both sides. In this respect my Case 3 is particularly instructive, for in it the disease has not progressed too far; we can see, as it were, degeneration in the making. It is unnecessary to repeat what has often already been noted, that the selective action of the morbid agent is by far the most striking characteristic of the disease—optic thalamus, internal capsule, and caudate nucleus intact, lenticular nucleus shrunken, atrophic, crumbling. It is true, of course, that in Case 1 slight disease of one optic thalamus occurred, and that the external capsule has been involved in more than one case; the caudate also is sometimes rather smaller than normal—*i.e.*, some-

what atrophic. But the contrast between the entire disintegration of the putamen and the conservation of the other ganglia is none the less striking. Let it not be supposed that this selective section is merely a question of vascular distribution. According to the latest and most accurate researches the lenticular nucleus has two, if not three, main sources of vascular supply, distinct from each other. Were we dealing with disease in a particular vascular distribution the structural changes would be quite different. Compared with the cavitation of the right lenticular nucleus (fig. 29) it is remarkable how well preserved are all the tissues round it. It is clear that no mere question of vascular supply will account for the steady disintegration of a collection of grey matter in one place, while other collections of grey matter in close proximity are unaffected. It is in my opinion possible that in the affected areas the degeneration of the vessels—their fragility and thinning or occasional thickening—may be in part secondary to the degeneration round them. This would certainly seem to be the case with some of the vessels round the lenticular cavities in Case 1. Although it is likely that the toxin, whatever it be, acts on the nuclei via the blood-stream, there are no signs of changes in the blood-vessels such as accompany thrombotic softening.

How, then, are the phenomena to be explained? Is there a direct chemical or other affinity between the nerve-elements of the lenticular nucleus and the presumed toxin? The fact of the restriction of the pathological process to that nucleus, at least to a far greater extent than in the case of the other basal ganglia, cannot be gainsaid. A good deal of light is thrown on this obscure subject, I believe, by an analogy of an interesting and instructive kind.

Within the last few years four German observers—viz., Beneke [88], Schmorl [91], Esch [89] and Pfannenstiel [90]—have described cases of a rare variety of icterus neonatorum, distinguished as icterus gravis neonatorum. This form of the disease is familial, occurs in the earliest days of life, and is fatal in a very short time, the infants rarely living longer than a week or two. They are acutely jaundiced; every tissue of the body would appear to be bile-stained, so acute is the process. Successive infants in a family may be affected. Now it is a remarkable fact that while the cases do not show any special nervous symptoms during life the distribution of the bile-staining in the cerebrum and central nervous system generally is curiously selective. Seeing that the infants are acutely and universally jaundiced, it is somewhat astonishing to learn, as remarked by all these writers, that in the brain the lenticular nucleus on each side, the corpus Luysii, the cornu Ammonis, the

nucleus dentatus and olives, the sensory nuclei of the medulla and pons, in particular the eighth and tenth (*not* the motor nuclei), are specially singled out and are stained a bright yellow—in the case of the corpus Luysii and the lenticular nucleus an intense yellow—while the cortex cerebri, the caudate and optic thalamus show only a faint tint or none at all.

This "Kernicterus," as the Germans call it, was found by Schmorl six times in 120 cases of icterus neonatorum; it is not, therefore, so exceedingly rare. The lenticular nucleus and corpus Luysii are specifically mentioned by all as being deeply stained, while the caudate nucleus and the optic thalamus escape; in other words, there is here a localized association of a poison, or whatever it is to be called, with particular nerve-cell groups, and this poison circulating in the system is associated with hepatic disease. In these cases there is no evidence of infection of any ordinary type; syphilis can be excluded. This disease, whatever be its origin, occurs in families, is fatal during the first few weeks of life, and is characterized by profound and generalized icterus; yet in the brain certain cell-groups are singled out, others are untouched. It is important to note that this is no mere question of staining of a matrix or interstitial tissue with bile-pigment, for *microscopically the bile-pigment is found in the bodies of the nerve-cells*, and in their immediate neighbourhood masses of pigment may be deposited.

Now in ordinary cases of jaundice in older people, from whatever cause arising, and in the jaundice of congenital bile-duct obliteration, no such selective staining of grey matter has ever been found, as far as I have been able to discover. The conclusion seems clear that familial icterus gravis neonatorum, of the Kernicterus type, is a highly specialized disease where a toxin presumably of hepatic origin exhibits an affinity for the lenticular nucleus and corpus Luysii, in addition to other smaller collections of grey matter, while it leaves the optic thalamus and caudate nucleus untouched, or practically so.

The analogy Kernicterus offers to progressive lenticular degeneration is therefore highly suggestive. I do not wish to overestimate the value of the analogy, however, and in drawing attention to it, and to the possibility of its opening up a new field of research, enough has been said at present.

(6) THE NATURE OF THE TOXIN IS UNKNOWN: IT IS ALMOST CERTAINLY NOT MICROBIAL.

There is no evidence that progressive lenticular degeneration is microbial in origin. Only the modern cases have been examined from

this point of view. In two of my cases there was abundant trace of infection of bacterial type, but there was every reason to suppose, at the same time, that this infection was terminal, and therefore of no pathogenic significance. The third case, although examined just as minutely for signs of bacterial invasion, was negative. Hence the idea that the disease is of microbial origin may be dismissed.

There is much in the disease for which further research is required. Its problems are easier to state than to elucidate. Whether, for instance, there is any connexion between the disease and the condition of the glands of internal secretion is at present obscure. In my Case 3 (the only case examined from this standpoint), the pituitary, thymus, and suprarenal glands were apparently unaltered. On the other hand, the thyroid was undoubtedly the seat of considerable change, the exact import of which I do not know. It will have been noted that in several cases the spleen has been enlarged, but it does not appear to show much definite change microscopically. With the onset of the disease in the female cases, menstruation became irregular and ceased. These are all subjects on which further investigation is needed.

The conclusions which have been come to, as indicated in this chapter, may be expressed as follows:—

Progressive lenticular degeneration, although it has frequently been recorded as occurring in families, is a disease almost certainly acquired, of a toxic or toxi-infective type. There are no grounds for supposing that the toxin is syphilis or parasyphilis. Certain facts suggest that it is elaborated in the liver, and that it acts, presumably *viâ* the bloodstream, on the corpus striatum. In icterus gravis neonatorum a poison, presumably of liver origin, has been found to have a specific action on the lenticular nucleus, corpus Luysii, and certain other small collections of intracranial grey matter. The exact nature of the morbid agent in progressive lenticular degeneration is unknown. It is in all probability not microbial. Possibly it is chemical and of the nature of a lipid.

CHAPTER VI.—PATHOLOGICAL PHYSIOLOGY OF THE MORE IMPORTANT SYMPTOMS.

THE symptoms which stand out conspicuously in the syndrome of progressive lenticular degeneration are involuntary movements, almost always of the tremor variety, muscular hypertonicity and contracture, dysarthria and dysphagia, and a degree of emotionalism, and they may be considered briefly in turn. The first three form a triad which is never wanting in a typical case of the disease.

(1) INVOLUNTARY MOVEMENTS: TREMOR.

In at least nine of the twelve cases accepted for purposes of analysis tremor was an early, a prominent, and a progressive symptom; in two others it was not quite so prominent, "clonic and tonic spasms" being specified as the type of involuntary movement present. For practical purposes, however, tremor—a regular rhythmical alternating contraction of muscular groups and their antagonists—is in the foreground of the clinical picture, and its pathogenesis is a matter of considerable interest.

An immense amount of research has been devoted to the question of involuntary movements, of which there are three main varieties, distinguished as athetosis, chorea,¹ and tremor. Many cases of a conflicting nature have been published, no doubt as the result, in part, of difficulty in distinguishing the varieties above mentioned. Yet, as a rule, they can be distinguished readily enough. Athetosis and chorea are involuntary movements of a different type from tremor, and sometimes they cannot be fully separated from each other. On the other hand, though tremor and athetosis occur together, they are, in my opinion, sufficiently distinct to be described apart.

In a consideration of the whole question it is essential to "think anatomically." Confusion becomes worse confounded unless anatomical details receive their due recognition. An independent analysis of a great number of recorded cases of involuntary movement has led me to the conclusion (which is accepted, I believe, by the majority of neurologists) that the anatomical area, in association with lesions of which involuntary movements occur, is more or less definitely limited to the basal ganglia, superior cerebellar peduncles (and possibly cerebellar nuclei), and mid-brain. A few cases, selected at random, will support this contention.

Thus, in athetosis, the lesion has been localized (1) in the corpus striatum (Anton [43], Berger [45], Oppenheim and Vogt [40]); (2) in the optic thalamus (Herz [17], Frey [13], S. A. K. Wilson—an unpublished case); (3) in the red nucleus (Halban and Infeld [16]); (4) in the cerebellum (Pineles [29]). The lesion of chorea (post-hemiplegic hemichorea) has been localized (1) in the corpus striatum (Schilder [32]); (2) in the superior cerebellar peduncle (Sander [31], Muratow [25]); (3) in the red nucleus (Bonhoeffer [10], Kolisch [21]). Tremor is caused by lesions (1) in the corpus striatum (Rhein and Potts [62], Démange [49], Eisenlohr [50], S. A. K. Wilson); (2) in the red nucleus (Marburg [24], Holmes [18], Van Oordt [27]); (3) in the

¹ By the term "chorea" is meant that type of involuntary movement which, occurring, e.g., after hemiplegia, resembles the movement of Sydenham's chorea more or less closely.

tegmentum (Bristowe [11]); (4) in the optic thalamus (Leyden [23]), &c. Many more examples might be quoted.

Although at first sight the conflicting nature of the evidence may appear far from encouraging, it requires to be examined more closely. Certain facts, it appears to me, stand out as proven and of prime importance.

(a) *The pyramidal tracts must not be too severely injured.* If they are, then no involuntary movements occur. With complete paralysis of voluntary movement involuntary movement is never seen. After a stroke, involuntary movements do not set in until volitional power begins to return. This is true both for athetosis and for tremor. More than one case is on record where the involuntary tremor of paralysis agitans has ceased owing to the occurrence of a stroke. Further, I have seen a case of infantile cerebral hemiplegia, with hemi-athetosis, where the patient was subject to Jacksonian fits on the affected side. An exhaustion-paralysis of the ordinary type used to follow these fits, lasting for about twenty minutes. During that time the involuntary movements invariably ceased completely. Such facts are of peculiar significance for my contention.

(b) *A lesion of the pyramidal system is not by itself sufficient to produce involuntary movements.* Innumerable cases of hemiplegia occur where involuntary movements are conspicuously absent. There is no case of involuntary movement on record pathologically in which the lesion did not involve, directly or indirectly, certain areas of grey matter at the base of the brain, or in the mid-brain.

(c) *The assumption, therefore, is strong that other, extrapyramidal, paths must be injured.* What are these extrapyramidal paths? There are two that concern us in this connexion, one afferent and the other efferent (*vide* fig. 99). The former is the cerebello-rubro-thalamo-cortical path, which is well recognized anatomically: from the nucleus dentatus, via the superior cerebellar peduncle, to the nucleus ruber of the opposite side, and thence to the inferior and external division of the optic thalamus, and so to the sensory and motor cortex. There can be no doubt that with lesions of this system certain involuntary movements are prone to occur. The latter is the lenticulo-rubrospinal system, which is perhaps less well known. The nucleus lentiformis is practically independent of the cortex, but has important descending connexions, via the ansa lenticularis, with the regio subthalamica, the corpus Luysii, and the nucleus ruber. From the latter the path is continued as the rubro-spinal tract of Monakow, to the anterior horns of the spinal cord.

To lesions of this system I attribute very important symptoms, as will duly appear. It is to be noted that there is a kind of "short-circuit" between the corpus striatum and the optic thalamus.

(d) The next point is, *Are the symptoms (involuntary movements) caused by irritation or by destruction of these extrapyramidal paths?* In this connexion the teaching of Hughlings Jackson [19] is of far-reaching significance. It will be remembered he held that positive symptoms could not be *caused* by negative lesions. Hence, as the clinical symptoms which form the present subject of discussion are essentially positive, they cannot be *caused* by destructive lesions. In this way it is possible to exclude destructive lesions (1) of the pyramidal path, and (2) of the extrapyramidal paths as a *cause* of involuntary movement.

But further, irritation, or rather, irritative lesions, of the extrapyramidal paths are not at all likely to provoke involuntary movements. Experimentally, the optic thalamus and corpus striatum are practically inexcitable. The type of nerve-cell of these ganglia is different from that of the excitable motor cortex. Moreover, it is difficult to conceive of a lesion remaining irritative for years, yet we know that involuntary movements may persist indefinitely. Again, excitation of the cortex never produces movements analogous to athetosis, or chorea, or tremor. We are, therefore, forced to the conclusion that—

(e) *Destructive lesions of the extrapyramidal paths in some way allow involuntary movements to occur.* As far as athetosis and chorea are concerned it seems to me, a priori, highly improbable that so complex a series of movements as those of athetosis could be produced by irritation of the optic thalamus or corpus striatum. As above remarked, nothing approaching them can be obtained by excitation of these ganglia. It must be concluded, I think, that the movements constituting athetosis are of cortical origin, and that they are in some way the result of structural or functional defects in the cerebello-rubro-thalamo-cortical path. Absence of normal cortico-petal impulses travelling via this path allows the movements of athetosis to occur. It is probable that not all lesions of the thalamus or of other stations in the system cause this failure of cortico-petal impulses, but it is clear, I maintain, that on this hypothesis the occurrence of athetosis from lesions at different levels can be reasonably explained, and thus not a few apparently divergent cases are brought into line. The exact area of the cortex to which go the fibres subserving this "inhibitory" function is not known, but there are grounds for believing that the intermedio-

precentral cortex plays a part in the production of the involuntary movements; in any case, the precentral cortex and the pyramidal path must be comparatively intact. If they are thrown out of gear completely the involuntary movements cease. It is possible, further, that certain corpus striatum lesions, as the result of some intimate association by striothalamic fibres, may occasion athétosis.

With tremor, the case is rather different. Experimental data from excitation of the cortex, corpus striatum and optic thalamus are uniformly negative. Karplus and Economo [20], however, have produced tremor by excitation of the nucleus ruber. From clinical and pathological evidence, it is probable that tremor is the result of disturbance of the efferent extrapyramidal path, the lenticulo-rubrospinal, which I have described. My view is that destructive lesions of this path remove a normal "inhibiting," or rather steadying, influence which the corpus striatum exercises on the anterior horn-cell. As a result of this removal, steady innervation of the anterior horn-cell is impaired, and the more the pyramidal path is innervated the more obvious does the tremor become; in other words, it increases with voluntary effort—a characteristic of the tremor in all cases of progressive lenticular degeneration. In accordance with this hypothesis, if the anterior horn-cell is not intact, if the pyramidal cortex or tract is severely injured, the tremor cannot be so obvious. If the pyramidal injury is profound, there can be no tremor.

It is conceivable, however, that the absence of the normal steadying influence of the lenticular nucleus may make itself felt via the striothalamic fibres on the external part of the optic thalamus, and so on the intermedio-precentral and precentral cortex. There may thus be a double action of the corpus striatum on pyramidal innervation—viz., directly on the anterior horn-cell and indirectly on the motor cortex. I am not at present prepared to develop this view further; but what has been already said may help to elucidate the pathogenesis of the tremor which is so striking a feature of progressive lenticular degeneration.

It is only in the sense which has been carefully explained above that involuntary movements are "of cortical origin." The position that tremor is caused by cortical irritation (see, for instance, Sharkey's [33] Goulstonian Lectures, 1886) must be abandoned. Homén's contention that tremor is to be regarded as the "Ausdruck einer Corticalreizung" is similarly indefensible. The pathological features of progressive lenticular degeneration lend support to the view which associates tremor with mid-brain and tegmental lesions generally (Holmes, Marburg), but

I have here elaborated a more inclusive hypothesis, which serves to explain certain other recorded cases in addition. I do not consider that the absence of obvious pathological changes in the red nucleus (beyond the increase in parasite glial cells) and Monakow's bundle in my cases of progressive lenticular degeneration, militates against the views here advanced. The gross lenticular disease and the degeneration of the ansa lenticularis are of course obvious; and I consider that defect of the nervous influx from the lenticular nucleus may determine a dynamic modification of the function of the rubro-spinal system without anatomical lesion.

(2) MUSCULAR RIGIDITY AND CONTRACTURE.

All of the series of twelve cases showed rigidity and contracture in greater or less degree. Muscular rigidity, therefore, may be taken as one of the cardinal features of the disease. It is necessary, however, to define the expression more accurately. I have used "rigidity" simply as a general term to indicate the condition of the musculature. What is meant, in exact terminology, is a condition of hypertonicity, involving all muscular groups alike. Even when the limbs are put into a position calculated to produce the maximum of relaxation, palpation of the muscles will convince the observer of their hypertonicity. They feel firm and hard, not of course always in marked degree, but nevertheless to an extent that cannot fail to be noticed. Moreover, on impressing passive movements on a given limb, at any joint, more particularly at the proximal joints, the observer will note that when he flexes passively the movement is resisted by the extensor antagonists, and when he extends, by the flexor antagonists. Thus the hypertonus becomes very manifest. Now it is clear that this condition is different from the ordinary spasticity of pyramidal lesions. In a spastic paraplegia it is usually found that when the lower extremities, which are stiffly extended on the bed, are passively flexed at the knees, the calf muscles are not really hypertonic; on the contrary, they are often curiously soft. The apparent stiffness, and the "sticky" gait, are the result of weakness of the flexors, their antagonists being by contrast hyperactive. This is true of the lower limb in many cases of ordinary pyramidal hemiplegia; the circumduction of the limb in walking is occasioned not by rigidity so much as by weakness of the flexors. The hypertonus of the muscles in progressive lenticular degeneration, then, is not the same as that which is met with in lesions of the pyramidal system. It must

not be forgotten, further, that with this remarkable hypertonicity the abdominal reflexes are not abolished, in a pure case, and the plantar response is flexor, while from the pathological standpoint no degeneration can be found in the pyramidal tracts. It may be definitely stated, therefore, that the condition of hypertonus is of extrapyramidal origin.

It is true that the factors governing muscle-tone are somewhat complicated. In the first place, there is no reason to suppose that in the present series of cases the hypertonus of the musculature is of myogenic origin. In my Case 3 the patient was able voluntarily to flex and extend muscles that were definitely hypertonic, long before true contracture set in. Neither clinically nor pathologically was there any evidence that the hypertonus was akin to the myotonia of Thomsen's disease, or of myotonia atrophica, where the sarcoplasm—the extreme motor periphery—is probably the seat of the disease.

Secondly, while tonus is a reflex phenomenon associated with integrity of the spinal reflex arc—posterior root, anterior horn-cell, anterior root—yet the pathological evidence of my own cases shows that the spinal cord was normal. In certain cases of syringomyelia a hypertonus of cord origin is seen in certain muscle-groups [69], and after lesions of the anterior cornual cells loss of tone is frequent, but in progressive lenticular degeneration another cause for the variations of tonus must be sought. It has already been pointed out that the hypertonicity is different from the ordinary spasticity of pyramidal lesions, which, according to Charcot and others—though this view is now somewhat discredited—results from removal of the inhibitory influence of an intact pyramidal system on the spinal reflex arc.

Thirdly, the association of the cerebellum with the maintenance of muscle tone is no doubt a close one. Atonia is frequent with cerebellar lesions (Luciani [73], Thomas [76], Babinski [66]), and, on the other hand, cases of cerebellar disease with acquired myotonia have been recorded (Levi[71]). I have seen two patients with so-called cerebellar fits in whom, after the tonic stage was over, there was a profound atonia of the musculature, as though the muscles that had been contracting were literally emptied of tone. But in the disease under consideration cerebellar symptoms are notably wanting, and pathologically the layers of the cerebellar cortex, as well as the cell-content of the nuclei, are apparently normal. Further, no definite anatomical lesion is to be found anywhere on the course of the cerebello-rubro-thalamo-cortical system already referred to, even if we are to assume that interference with its

integrity might be a conceivable cause of hypertonus of the skeletal muscles.

Fourthly, the existence of higher centres which are concerned with the maintenance of tone must be conceded. There is increasing evidence in favour of the view that muscular tonus depends, to some extent at least, on the reaction between the basal ganglia, and between them and the cortex. I do not think that there is any satisfactory evidence to place such tone-centres in the medulla, pons, locus niger, crus, &c. Thus in certain cases of hemiplegia the paralysis may be minimal, while the affected limbs become peculiarly hypertonic, a hypertonicity which involves all muscular groups alike. The condition has been called "hemitonia apoplectica" (Bechterew [67], Pfeiffer [75]), and more than one case has come under my own notice. As far as I am aware no pathological examination in this condition has yet been made, but that the hypertonicity is of central origin is patent. Again, a case has been recorded by Etienne [68], in which a post-hemiplegic "hemi-tonoclonic syndrome" of a striking kind occurred in a woman, aged 49, with a right hemiplegia. There was a severe degree of volitional paralysis of the right side, but the muscles were actually hypertrophied from overaction of an involuntary nature. There were more or less constant attacks of violent hypertonic spasmodic contractions of the muscles on that side, which frequently began by marked involuntary tremor, passing into tonic spasm. Rhythmic clonic tremor of the right leg was almost unceasing. In addition to the ordinary contracture of hemiplegia there was active tonic contracture, coming in "attacks." Etienne employs the phrase, "a permanent muscular erethism." The resemblance between this case and the phenomena described in one or two cases of the acute variety of progressive lenticular degeneration, as well as in one of Homén's cases, is very intimate and instructive. There was no *post-mortem* examination in Etienne's case, but of the central origin of the hypertonicity no doubt can be entertained.

Further, cases of hemiplegia presenting the converse of this are occasionally met with, viz., cases in which the affected limbs remain permanently atonic—apart, that is, from mere paralysis, and in which no contracture develops. The pathology of these cases is apparently unknown.

From all these facts it may reasonably be assumed that there are cerebral centres concerned with the maintenance of tone. It is also, I think, undeniable that symptoms of this kind require the involve-

ment of nerve-cells for their continuance, and cannot be accounted for by simple irritation of pyramidal fibres.¹

It may be asked at this point whether there is any close association, pathogenically, between the tremor and the hypertonicity. The two phenomena proceed *pari passu* in the disease we are considering, as a rule, and are observed to vary in intensity from time to time, as well as occasionally to come in "attacks." In the majority of cases of tremor which I have seen it is associated with a certain degree of hypertonus of the muscles. Hughlings Jackson used to say that tremor is rigidity "spread out thin," and conversely, that rigidity is tremor "run together." Be this as it may, paralysis agitans is a disease in which muscular rigidity and tremor are intimately linked, and in which, as a rule, the degree of one is in inverse proportion to that of the other. When, therefore, in at least two distinct morbid conditions such an association is found, the suggestion of these two symptoms having a common origin comes within the realms of possibility.

In view of the occurrence of changes in tonus from central disturbances, the suggestion which I make may be expressed as follows: Disease of the corpus striatum, and in particular of the lenticular nucleus, especially if it is bilateral and of sufficient extent, removes a steadying or "inhibitory" influence which that nucleus normally exerts on the corticospinal paths. There is good reason to believe that this influence is exerted either via the thalamus on the cortex or via the lenticulo-rubrospinal system on the anterior horn-cell. Absence of this "Hemmung" makes the cortical motor-cells react in such a way that one of the results is increase of tonicity of all the muscles reached by the pyramidal tracts. The function of the motor cortex is interfered with to the extent of the development of this hypertonus, with which is coupled motor weakness, but there is no paralysis of innervation. It is probable, further (as explained in a previous section), that absence of a steadying influence on the anterior horn-cell, exerted via the red nucleus, is accountable more particularly for the tremor which is so characteristic a feature of the disease, and which is increased by volitional innervation of the corticospinal path.

It may be that variations in the nature of the change of the normal afferent impulses to the sensorium from the optic thalamus will explain the different ways in which the cortex will react—i.e., either by

¹ There is evidence to show that certain lesions of the frontal lobe and of the corpus callosum are connected with the clinical phenomenon of "tonic perseveration" in the opposite limb, but this condition is not of the same nature as the hypertonus under discussion.

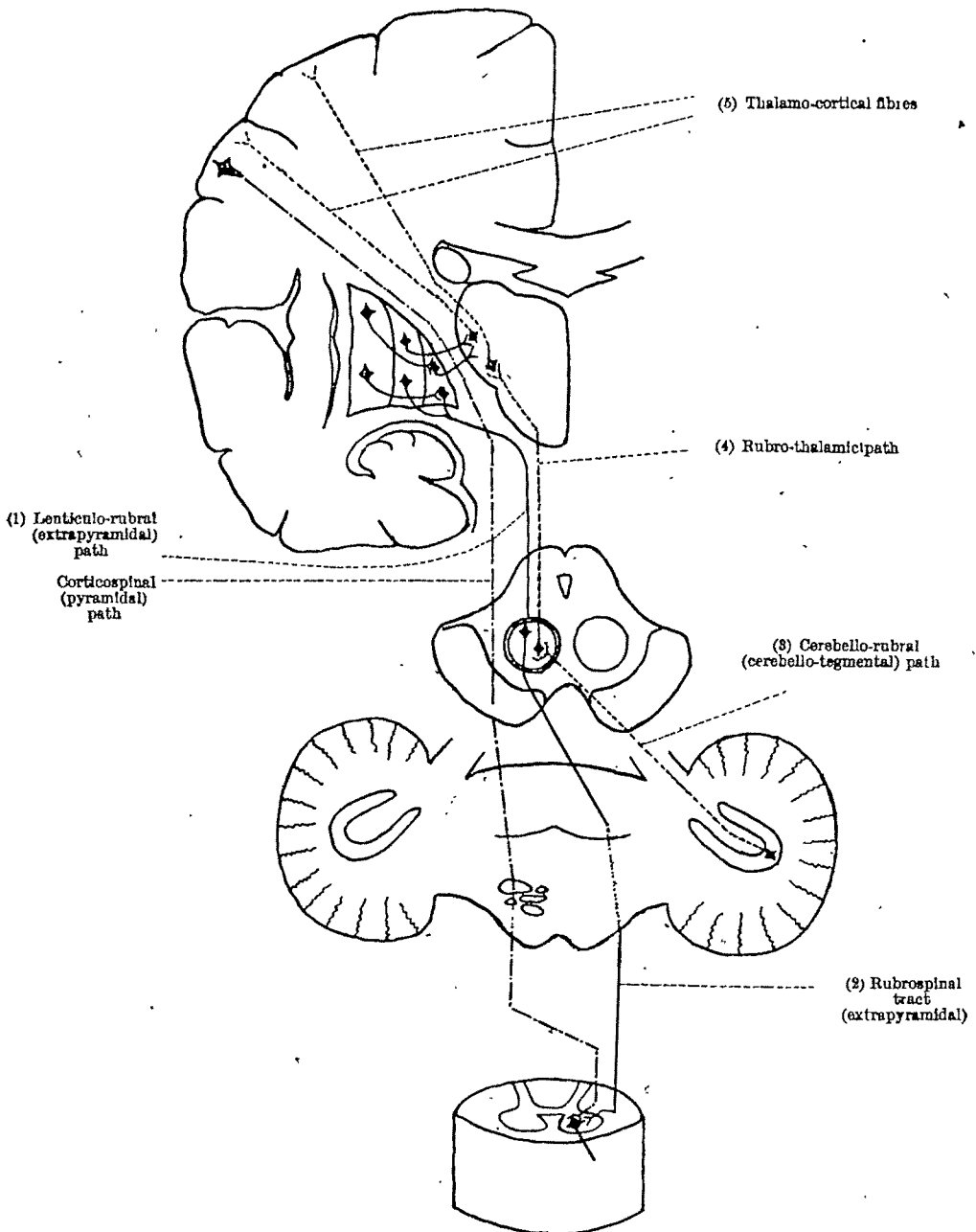


FIG. 99.—Diagram to show the relations of the pyramidal and extrapyramidal systems, and the afferent cerebello-cortical system. (1) and (2) constitute the lenticulo-rubrospinal path (efferent); (3), (4), and (5) the cerebello-rubro-thalamo-cortical path (afferent).

involuntary movements or alterations in myotonus, or both. It seems tolerably clear that interruption of centripetal impulses causes arrhythmical and asymmetrical innervations from the cortex, but, as remarked above, in the case of the thalamus the area affected, either directly or indirectly, as a result of which cortical innervation is disturbed, is probably limited. In the case of disease of the lenticular nucleus, such an indirect causation must be postulated, for it has practically no direct connexions with the cortex at all.

Athetosis and chorea differ from tremor in that the former, at least, is in most cases associated with muscular hypotonia (but see [70]). Athetosis, then, is an instance of the coupling of involuntary movement with diminished tonicity, and its pathogenesis, although it follows the lines which have been sketched, must be somewhat different. Wherein this difference consists, anatomically, is in the present state of our knowledge uncertain, but because the involuntary movements and the state of muscular tonus differ from what obtain in progressive lenticular degeneration, the general hypothesis enunciated above is not thereby invalidated.

The occurrence of contractures in extrapyramidal motor disease is noteworthy. With the exception of paralysis agitans, the disease which is here described is the first, apparently, in which contracture has been shown to occur with an intact pyramidal system. It is highly probable that the fixity of the limbs in the contracture-attitudes already described (the result of the absence of impulses from the corpus striatum to the cortex) has facilitated the development, at a subsequent stage, of true contracture. Metabolic changes and the resulting muscular wasting have also, no doubt, much to do with the appearance of this condition.

(3) DYSARTHRIA: DYSPHAGIA.

Dysarthria is the third of the cardinal features of progressive lenticular degeneration. For its pathogenesis two views may be advanced.

Brissaud [77] was the apostle of the theory which placed subsidiary motor centres for articulation and deglutition in the putamen. According to this view, the dysarthria that is so prominent a symptom of pseudobulbar paralysis is not due to implication of capsular fibres, but to involvement of these secondary centres in the putamen, or of the fibres coming from them. Apart, however, from the fact that there is no experimental evidence to support this view, and that there are certain histological difficulties in the way of its

acceptance, the clinico-pathological method has demonstrated its erroneousess. The reader is referred to the researches more particularly of Comte [78] for full discussion of the evidence. Many years previously, however, Ross [63] had come to identical conclusions. In pseudobulbar cases the cause of the dysarthria and dysphagia is involvement of the motor fibres from the lower motor cortex (operculum), somewhere in their course skirting the lenticular nucleus, via the genu of the capsule and the inner section of the crus, to the corresponding nuclei of the medulla.

Now, in my Case 1 it is true that the genu of the capsule is definitely, though slightly, affected on one side. But it is important to note that in Case 3 an equal degree of dysarthria and dysphagia occurred; yet there was complete integrity of the internal capsule and pyramidal tract generally. It is necessary to advance, therefore, another explanation for the production of these symptoms. It seems most natural to associate the dysarthria with the general hypertonicity of the skeletal musculature. The muscles of the throat, palate, and tongue were just as involved in the overaction of the pyramidal system as any of the other muscles of the body. Volitional control over them was just as feeble and imperfect—in fact, the smallness of the movements concerned in articulation is a good reason for the early appearance and profound degree of dysarthria which characterize all the cases. This view, moreover, brings these symptoms into line with certain others. In the clinical histories it will be remembered that several observers, including myself, noted considerable variability in the dysarthria and dysphagia from time to time. Were these symptoms due to structural defects of their innervating neurones, this variability could not, in my opinion, be explained satisfactorily. If it is regarded, however, as due to variable disturbance of a steady influence, exercised by a large ganglion that is slowly degenerating, the fact of the articulation being better at one time than another is not to be wondered at.

If the disease advances, and the patient lives long enough, it can be readily understood that the "faisceau geniculé" may eventually become affected on one or both sides, in which case the anarthria and dysphagia become those of a true pseudobulbar paralysis. In that case the patient would have definite paralysis of the palate and tongue. It may be mentioned again, however, that in my own cases neither the palate nor the tongue was paralysed in reality, in spite of the profound degree of anarthria. Thus the view of the pathogenesis of these symptoms here advanced is the only one that explains the clinical observations satisfactorily. (See also p. 453.)

(4) EMOTIONALISM.

A degree of emotional overaction, in the shape more particularly of involuntary laughing, is a frequent, though not a constant, feature of the disease. The association of "rire" and "pleurer spasmodique" with disease of the basal ganglia has long been recognized; it is very common in double hemiplegia and pseudobulbar palsy, and occasionally occurs in simple hemiplegia. In my own cases I could not always determine that the involuntary laughing was associated with any definite affective tone; on some occasions, at least, the patients did not appear to experience the emotion which their musculature seemed to express.

The exact relation between the clinical phenomena and the pathological changes—indeed, the exact site of the latter—have not been elucidated with any completeness. Following Nothnagel, it has been commonly taught that involuntary emotionalism occurs in disease more particularly of the optic thalamus; but, assuming this is the case, the pathogenesis of the condition is not thereby made more obvious. In progressive lenticular degeneration the thalamus is not involved directly; there is a notable loss of striothalamic fibres, by which, presumably, some functional interaction of these two ganglia is maintained. The striothalamic fibres go mainly to the outer part of the thalamus, which is the section of that ganglion more definitely connected with the sensory system and with the cerebello-rubro-thalamic system. But it must not be forgotten that involuntary laughing is a positive symptom, and cannot be caused by a negative lesion. It is on a par with the other symptoms indicative of defect of cortical control, and it may be supposed that a sensory stimulus either reaches the cortex via the thalamus, and there produces an unusual effect through impaired pyramidal function, or that by a short-circuit from thalamus to corpus striatum, and so to anterior horn-cell, or rather to its pontine analogue, an uncontrolled innervation of the latter is effected. In any case I do not consider that either optic thalamus or corpus striatum can be regarded as a "lower motor centre" in any sense analogous to the motor cortex; the *only* "lower motor centre," or "subcortical motor centre," which exists is the anterior horn-cell of pontine, bulbar, or medullary grey matter.

CHAPTER VII.—SYNDROME OF THE CORPUS STRIATUM.

THE lenticular nucleus, and corpus striatum generally, occupy a considerable area in the middle third of the cerebral hemispheres; the arrangement of cells and fibres in them is somewhat complicated, and it is contrary to physiological conceptions to suppose that ganglia of such a size should be unimportant from a physiological standpoint. It is, however, undeniable that our knowledge of the functions and pathology of the corpus striatum has hitherto been curiously indefinite. On the one hand, small lesions of that body have often proved to have been entirely without effect, from a symptomatological point of view, and even larger lesions have sometimes, apparently, failed to reveal themselves by any recognizable symptoms during life. On the other hand, uncomplicated involvement of the corpus striatum is a comparative rarity, and the proximity and close relationship of the corticospinal paths have led observers to attribute to impairment of the function of the latter any symptoms which otherwise might have been associated with the lesion in the former region. For these, among other reasons, the prevailing opinion on the physiology of the corpus striatum has been one of uncertainty. Thus Monakow, in the latest edition of his well-known "Gehirnpathologie," is forced to adopt a negative attitude. "In spite of the investigations of numerous experimenters, we know as little of the clinical effects of lesions of the lenticular and caudate nuclei, or as much, as Nothnagel did twenty-five years ago."

In the disease which I propose to designate progressive lenticular degeneration three desiderata are fulfilled on which the establishment of a corpus striatum symptom-complex would seem to depend. The lesions are sufficiently large, in the first place; of sufficiently long duration, in the second place; and in the third they are confined to the ganglion itself. My Case 3 offers a perfect opportunity of differentiating lenticular from corticospinal symptoms. With integrity of the internal capsule and pyramidal paths generally there is bilateral degeneration of the lenticular nucleus, which reveals itself by a train of clinical symptoms amply corroborated by the results of the investigation of a number of other cases, all collected in this paper, so that a general review provides a striking confirmation of the general statement.

The syndrome of the corpus striatum, therefore, which is here put forward, may be expressed as follows:—

In pure, uncomplicated, bilateral lesions of the lenticular nucleus, and more generally of the corpus striatum, provided they are of sufficient

size and of adequate duration, the clinical symptoms are bilateral involuntary movements, practically always of the tremor variety; weakness, spasticity or hypertonicity (sometimes spasmodic contractions) and eventually contracture of the skeletal musculature; dysarthria or anarthria and dysphagia, and a degree of emotionalism; but without any sensory disturbance, without any true paralysis, and without any alteration in the cutaneous reflexes. If the abdominal reflexes are absent (apart from muscular rigidity) or the plantars of extensor type, then the syndrome is no longer pure.

In view of this syndrome, thus differentiated for the first time from a study of progressive lenticular degeneration, the loose way, sometimes adopted, of considering "signs of organic nervous disease" and "signs of pyramidal nervous disease" as one and the same thing must be definitively abandoned. Pure cases of progressive lenticular degeneration show no signs of pyramidal defect of function (as estimated by the reflexes), but the disease is none the less one of the most serious organic diseases of the nervous system that the neurologist is likely to encounter. It is unfortunate that there is no expression in common use to indicate extrapyramidal motor disease.

It has been already remarked that the resemblance between progressive lenticular degeneration and paralysis agitans is considerable. In the latter there is a symptom-complex of tremor, rigidity, and weakness; sometimes there is a degree of emotional overaction, and, as in early cases of the former disease, the patient's utterance is monotonous and sometimes dysarthric; "*il a perdu le chanson du langage*," to use a picturesque French expression. The articulatory and phonatory defects of the Parkinsonian are in my opinion the result of rigidity of the corresponding musculatures, and not due to a true pseudobulbar condition. Hence the relation between the two conditions is very close, that is to say, as far as the clinical symptoms are concerned, for there are differences of age and etiology and duration which are obvious enough. It might be expected, then, that the pathology of the two conditions, or at least the localization of the lesions, should be more or less identical. Hitherto, in paralysis agitans, no certain pathology has been demonstrated. But within recent years various data have accumulated to show that its lesions will probably be found in the basal ganglia and regio subthalamica. What is paralysis agitans but an extrapyramidal motor disease? Its pathology must therefore be looked for along the lines that have been indicated in the last chapter. In this connexion it is of great interest to note that Jelgersma [87] has found bilateral

degeneration of striothalamic fibres and of the lenticular bundle of Forel in that disease. That investigation in this field will be amply repaid I am firmly convinced. We need not look for gross anatomical lesions in paralysis agitans. It has been pointed out above that dynamic modifications of function may be produced without much anatomical change, and such may well prove to be the case in Parkinson's disease.

The syndrome of the corpus striatum here given differs in some important respects from other corpus striatum syndromes recorded in recent years by different observers, who have based their conclusions on pathological material of somewhat varying nature. At the same time it presents close analogies to one of these, to be referred to immediately, which, in my opinion, is best entitled to consideration.

(1) Piazza [41], basing his conclusions on the case of an old man aged 74, a senile dement, in whom generalized cerebral arteriosclerosis was found *post-mortem*, with bilateral softening of the putamen, as well as on a number of recorded cases, describes a syndrome of the lenticular nucleus, comprising slight paresis, dysarthria, trophic and sensory disturbances. If the middle section of the putamen is involved there is paresis of the limbs; if the lesion is outside this, choreic and athetoid movements may result.

Cases of this description are plainly unsatisfactory from several points of view, and the syndrome itself contains features which cannot be accepted as characteristic of lenticular lesions.

(2) Franceschi [35] describes a lenticular syndrome consisting of forced laughing and crying, dysarthria and double hemiparesis, and assumes that through the lenticular nucleus run the thalamo-cortical paths concerned in emotional expression. In his case, one of bilateral lenticular softening, the anterior limb and genu of the internal capsule were implicated on the right side, and part of the posterior limb on the left side.

Apart from the fact that anatomical evidence is against the assumption just quoted, no case can be considered free from objection where the corticospinal paths are involved as well.

(3) Mingazzini's [39] lenticular syndrome consists of slight facial and limb paresis on the opposite side, exaggeration of the tendon reflexes, anisocoria, sometimes atrophy of the extremities, and slight disturbances of objective sensibility; if the posterior four-fifths of the left lenticular nucleus is involved, then dysarthria or anarthria is superadded. If the outer third of the ganglion is diseased, the "*pseudomelia paræsthetica*" of Bechterew [44] may occur.

This syndrome, to the inclusion of certain features of which I cannot consent, has been quite recently enunciated by its author. It is based on the study of certain cases of cortical softening, Rolandic and otherwise, where some atrophy of the lenticular nucleus was found on the same side. When the upper and middle thirds of the precentral gyrus are destroyed, as in one of his cases, it is difficult to see how lenticular and corticospinal symptoms can possibly be differentiated.

In an earlier communication, Mingazzini [38], basing his researches on some thirteen cases, claimed that the lenticular nucleus is a motor organ of some kind, that even a small lesion of it never fails to manifest itself by motor disturbances, and that it is subdivided as is the cortical motor zone. He stated that the usual form of motor disturbance is a dissociated paresis or paralysis, sometimes with "irritative" symptoms, as a rule in the shape of tremor. He assumed that there are fibres from the motor speech cortex to the putamen, and from the putamen to the pontine and bulbar motor nuclei.

There are certain difficulties in the way of accepting these views, and the anatomical assumptions are open to criticism. There is, further, no unequivocal evidence that the lenticular nucleus may be subdivided as is the cortical motor zone. Involuntary movements are not produced by "irritation," while true paralysis does not result from disease of the putamen or globus pallidus. Mingazzini does not separate the pyramidal from the extrapyramidal symptoms as I have endeavoured to do, nor does he utilize the cutaneous reflexes as an aid in the matter.

(4) Dana [34] has published some cases of acute gas poisoning, where death has resulted in the course of a very short time. In some of the cases the lenticular nuclei were found *post-mortem* to be the seat of an acute hæmorrhagic softening. From these cases he concludes as follows:—

"The corpus striatum has not any independent or specific motor function. It probably has some supplementary motor function, especially in connexion with articulation. It may have some control over the bladder (double lesions). It seems to have some control over vasomotor and trophic conditions of the skin. It has no thermic centre. It may have some supplementary and associative psychic function, so that lesions affect memory and initiative. In severe gas poisoning there is a double softening of the lenticular nuclei, due to thrombosis of 'the artery of cerebral thrombosis,' and there result vasomotor and gangrenous conditions of the skin, so that these conditions in connexion with a history of coma from gas poisoning form a group of symptoms called 'the syndrome of the corpus striatum.'"

Apart from the indefiniteness of Dana's conclusions, why coma, vasomotor palsy, and gangrene, the result of acute gas poisoning, should be dignified as a "syndrome of the corpus striatum" I am at a loss to understand.

(5) Mills and Spiller [37], from an analysis of some eleven personally observed cases, not a few of which are complicated by other—i.e., extra-lenticular—lesions, find it difficult to form positive conclusions as to the symptomatology of lesions of the lenticular nucleus. They state *inter alia* that:—

Lesions restricted to the lenticula apparently do not cause sensory symptoms; speaking generally, the nucleus may be regarded as a motor organ; the left nucleus probably contains centres which are concerned with the "movements that make speech possible"; destructive lesions of certain portions of the nucleus probably cause a paresis of the limbs or face, but it differs from that produced by capsular lesions, not being so severe or characteristic.

These authors do not refer to involuntary movements, nor to hypertonicity or rigidity, nor to the condition of the reflexes. "Lenticular centres concerned with the movements which make speech possible" is an ambiguous expression the exact purport of which is not clear.

(6) Oppenheim and Cécile Vogt [40] have described two cases (mother and daughter) of "congenital infantile pseudobulbar paralysis," in one of which a *post-mortem* examination showed a bilateral atrophic marbled condition ("état marbré") of the corpus striatum, including the caudate nucleus, the putamen and the globus pallidus. The internal capsule was intact—was, indeed, rather hypertrophied. The clinical symptoms were spastic contracture of the limbs, dysarthria, choreo-athetoid involuntary movements of the limbs and facial musculature. The muscles of articulation, phonation, deglutition, and mastication were all in a condition of spastic weakness; the eye muscles were normal; saliva escaped from the lips. Freund and Cécile Vogt [36] have also recorded the case of an old woman, aged 77, with somewhat analogous clinical symptoms, dating from the development of a hemiplegia on the right side in infancy, and in this case a similar but less advanced atrophic "marbled condition" of the corpus striatum was found. The latter investigator has also had the opportunity of examining two other cases where the same curious pathological change was discovered.

Basing her conclusions on this material, Madame Vogt [42] has elaborated and published quite recently a syndrome of the corpus

striatum¹ consisting of spasmodic involuntary movements (athetoid), tremors, associated movements, emotionalism, without paralysis or with little paralysis, without sensory changes, and with no impairment of intelligence.

Although the actual pathological condition in these interesting cases is different from that of progressive lenticular degeneration, and although the clinical symptoms are not entirely identical, the localization of the morbid process is the same, and, moreover, the corticospinal paths are apparently intact. Hence the support which these cases furnish to the hypotheses which I have endeavoured to sustain in this paper is particularly gratifying. The syndrome published by Madame Vogt is the first in which the main function of the corpus striatum, as I believe, has been differentiated from that of the pyramidal system, and it corroborates to a considerable extent the views which I have formulated independently during my research on progressive lenticular degeneration. The syndrome which is furnished by that disease presents in its main features close analogies with that of Madame Vogt. We have involuntary movements, spasmodic contractures, dysarthria, emotionalism, without true paralysis, and without sensory changes. My cases, however, do not show associated movements, nor any type of athetosis. These differences are important, for progressive lenticular degeneration is a disease *sui generis*, and is not to be considered a variety of "athétose double." Madame Vogt holds that her syndrome of the corpus striatum is an "athétose double pure," but I am more inclined to associate tremor than athetosis with the syndrome, for reasons already given, and, moreover, progressive lenticular degeneration is in some respects better calculated to exemplify extrapyramidal disease, inasmuch as the abdominal reflexes are preserved and the plantars are flexor, whereas Madame Vogt acknowledges the difficulty, in her athetoid cases, of determining whether the plantar response is flexor or extensor.

That observer does not enter into the question of the pathogenesis of the symptoms, as has here been attempted; in what way the corpus striatum exercises its "inhibition" is not discussed by her; but the harmony between Madame Vogt and myself as to this "inhibitory" action of the corpus striatum, as to the occurrence of involuntary movements in its absence, and as to the preservation of sensibility, is complete. Madame Vogt holds that in the corpus striatum are certain

¹ "Nous en sommes ainsi amenés à construire un syndrome du corps strié consistant essentiellement en spasmes, plus ou moins accompagnés de mouvements athétosiques, d'oscillations rythmiques, de mouvements associés, de rire et de pleurer spasmodiques, sans (ou presque sans) troubles paralytiques, sans troubles de la sensibilité et sans troubles de l'intelligence: en d'autres termes, une athétose double pure."

"centres," lesions of which will produce a pseudobulbar paralysis, and she therefore finds herself in accordance with Brissaud and others [79] on this matter. I have shown, however, on a previous page, that a spastic anarthria and dysphagia may result from bilateral lenticular disease, closely resembling, but not identical with, a true pseudobulbar paralysis, seeing that the palatal and pharyngeal reflexes are preserved, and that the patient has still the possibility of a certain volitional innervation of the palate, pharynx and tongue. It is not, therefore, necessary to postulate these "centres," which, as has already been pointed out, are for other reasons improbable.

Other writers who have described cases approximating in one way or another to the syndrome furnished by progressive lenticular degenerations may be briefly mentioned.

Anton [43] has described the case of a boy, aged 9, who suffered from chronic choreo-athetoid movements of the limbs and of the face (grimacing, &c.), marked associated movements, dysarthria, and involuntary attitudes of the extremities; in the lower limbs the involuntary movements, according to the author's description, were more of the nature of tremor.¹ *Post-mortem*, bilateral atrophy and disintegration of the putamen were found, possibly of the "état marbré" type; the thalamus and internal capsule were noted as being intact. This case falls more into the category of so-called "athétose double," and presents close resemblances to the cases recently described by Oppenheim, Freund, and Madame Vogt. Anton considers that the involuntary movements are not the direct result of the destructive lesion, but that the latter removes normally acting inhibitory influences on innervation, acting downwards by a supplementary path, presumably on the anterior horn-cell. He thinks that emotional and associated movements are related to disease of the optic thalamus.

Anton's case, however, and those of the other German observers (above referred to) are not entirely identical, for Anton states definitely that the tonus of the muscles in his case was not conspicuously altered ("der Tonus der Muskulatur war nicht merklich verändert"), whereas in the others, especially Oppenheim's, attacks of spasm of long duration were frequent, forcing the limbs into contracture-attitudes, just as in some of my cases. They are alike, however, in the occurrence of associated movement and of athetoid involuntary movements, which do not occur at all in progressive lenticular degeneration. In my

¹ "Die Zehen fast rhythmisch einander entfernt und genähert worden. In der Muskulatur des Beines nahm die Unruhe mitunter den Charakter eines clonischen Erzitterns an."

opinion the tremor which the German cases showed (Anton, Oppenheim), such as it was, ought to be coupled with the lenticular disease rather than the athetosis, the likelihood of whose origin at various levels on the afferent cerebello-thalamo-cortical path has been sufficiently alluded to. The question of dynamic alteration of thalamic function as a result of corpus striatum disease is an important problem, which has not yet been seriously approached. In any case "athétose double" and progressive lenticular degeneration are different diseases and should be kept separate.

Rhein and Potts [62] have published a case of post-apoplectic tremor from symmetrical areas of softening in both lenticular nuclei and external capsules. The tremor—"alternate flexion and extension at the elbow and wrist, the hand being supinated: the movements were almost constant, only ceasing for a time if his attention was distracted"—was present on the right side only. The authors consider that the lesion on the right side may not have been large enough to cause tremor.

Landouzy [57] has recorded a case of right-sided "athetosis" from the age of 2, in a woman aged 32. The right arm was in a typical hemiplegic attitude, and looked to all appearance fixed and contractured, yet all voluntary movements could be performed slowly—"as if with regret"—so that complete extension at all joints was possible. There was no true contracture. In this respect the case bears an intimate relation to my own lenticular cases. The involuntary movements, described as athetosis, were "petits, faibles, lents, mais incessants." The lesion was an old softening of the left lenticular nucleus, enclosing in its centre a calcareous mass of the size of a haricot bean. The internal capsule was untouched.

Démange [49] describes the case of an old man aged 75, with right hemiplegia, and later a progressive left hemiplegia. On the right side was a rhythmical tremor exactly like that of paralysis agitans, and a similar though slighter tremor subsequently developed on the left side. In this case there was a bilateral softening of the lenticular nucleus, and the internal capsule was said not to be involved on either side.

A case has been put on record by Eisenlohr [50], in an old man aged 73, of paralysis of the lower face on both sides, dysarthria, diminution of motor power in the arms, great feebleness of the lower extremities, "which were seized with tremor on any attempt at walking, or on passive movements of them." *Post-mortem* a cystic cavity was found in the anterior part of each corpus striatum.

I am sorry not to have been able to consult the original description

of a case recorded by Löwy [60], where muscular rigidity, like paralysis agitans, but without tremor, followed bilateral softening of the corpus striatum. The title of the paper is suggestive: "Symmetrische Erweichungsherde beider Hemisphären im Kopfe des Nucleus caudatus und in äusserem Gliede des Linsenkerns, mit Muskelrigidität."

I have gone over a great number of other cases of lesion involving the lenticular nucleus that have been recorded, but from the special point of view of distinguishing pyramidal from extrapyramidal symptoms they are all unsatisfactory. Certain cases appear to be negative (Hutchinson [56], Bramwell [46]); in others the internal capsule is affected, or the lesions are too recent or multiple, or there is generalized arterial disease, or the descriptions, clinically and pathologically, are not given in sufficient detail (Hebold [55], Canfield and Putnam [47], Fuller and Browning [52], Lépine [58], Ross [63], Reichel [61], Berger [45], Schilder [32], van Gehuchten [53], Ferrazini and Paoli [51], Czyhlarz and Marburg [48], Weir Mitchell [65], Grasset [54], &c.).

A number of cases of the ordinary pseudobulbar syndrome, with a more or less definite double hemiplegia, have been recorded. The majority of these have consisted pathologically of a bilateral lesion in the corpus striatum with involvement of the corticospinal paths (Weisenburg [86], Marshall and Jacob [83], &c., &c.). Some cases presenting this syndrome have had lesions apparently confined to the corpus striatum (Ross [63], Leresche [82]). In so far as these cases present symptoms analogous to certain of those of progressive lenticular degeneration they are of value; but from the pathological point of view only the method of serial section will suffice to indicate the exact extent of the lesion, and in cases of this description—i.e., where the difficulty is to distinguish between corpus striatum and corticospinal symptoms—the examination must be considered incomplete if this method is not employed. Some of the above cases were not examined microscopically, and the others are unsatisfactory for the reason just given. I have not referred to cases without pathological examination. A clinical case, however, of pseudobulbar palsy occurring in a child (Raymond and Lejonne [84]) may be noted, as in some ways it resembles progressive lenticular degeneration.

CHAPTER VIII.—CLINICAL CONCLUSIONS.

(1) Progressive lenticular degeneration is a disease of the motor nervous system, occurring in young people and very often familial. It is not congenital or hereditary.

(2) It is progressive and fatal within a varying period; acute cases may last only a few months; one chronic case has as a maximum continued for seven years; the average duration of chronic cases is four years.

(3) It is characterized by a definite symptom-complex, whose chief features are: generalized tremor, dysarthria and dysphagia, muscular rigidity and hypertonicity, emaciation, spasmodic contractions, contractures, emotionalism. There are also certain mental symptoms, either transient and such as one sees in a toxic psychosis, but not severe, or more chronic, consisting in a general restriction of the mental horizon, and a certain facility or docility without delusions or hallucinations, and not necessarily as progressive as the somatic symptoms. The mental symptoms may be very slight and are sometimes absent.

(4) In pure cases the affection constitutes an extrapyramidal motor disease, for the reflexes are normal from the point of view of the function of the pyramidal tracts.

(5) The neurological symptoms constitute a syndrome of the corpus striatum, which has not hitherto been differentiated in this disease.

(6) In some ways the disease bears a resemblance to paralysis agitans, and throws light on the problem of that affection.

(7) Although cirrhosis of the liver is constantly found in this affection, and is an essential feature of it, there are no signs of liver disease during life.

PATHOLOGICAL CONCLUSIONS.

(1) The chief pathological feature of the disease is bilateral symmetrical degeneration of the putamen and globus pallidus, in particular the former.

(2) This degeneration is the sequel to the selective operation of some morbid agent on the cells and fibres of the putamen and lenticular nucleus generally. The caudate nucleus is often somewhat atrophic, but never to the same extent, while other large collections of grey matter in the immediate neighbourhood of the lenticular nucleus—e.g., the optic thalamus, which has partially the same blood supply—is not affected at all in a pure case unless it be indirectly, and to a very slight extent.

(3) The morbid agent is probably of the nature of a toxin.

(4) A constant, essential, and in all probability primary feature of the pathology of the disease is cirrhosis of the liver, not syphilitic or alcoholic; it is multilobular or mixed in type, always pronounced, but presenting a varying pathological picture of necrosis, fatty degeneration, and regeneration.

(5) It is probable that the toxin is associated with the hepatic cirrhosis, and may be generated in connexion therewith. An important analogy may be drawn from the occurrence of "Kernikterus" in certain cases of familial icterus gravis neonatorum, where in spite of the universal bile-staining of the tissues of the body certain collections only of grey matter in the brain show a marked affinity for the circulating poison, while others do not. The parts that are stained deeply are in particular the nucleus lenticularis and the corpus Luysii (among others), while the optic thalamus, for instance, is scarcely stained at all.

(6) The pyramidal tracts are intact from Betz-cells to muscles in a pure case; occasionally certain secondary changes occur of limited significance.

(7) Certain secondary degenerations in the subthalamie region, of physiological importance, follow on the lenticular disease.

PHYSIOLOGICAL CONCLUSIONS.

(1) The corpus striatum exercises a steadying effect on the action of the corticospinal system.

(2) This is effected either by the lenticulo-rubrospinal system, or more indirectly via the optic thalamus and its cortical connections.

(3) When this influence is impaired pyramidal function is affected in its turn, and is seen in hypertonicity or rigidity, as well as in tremor on voluntary movement.

(4) There is not, however, any paralysis in the strict sense.

(5) The direct connexion of the corpus striatum with the cortex is minimal.

(6) There is no necessity to postulate articulatory "centres" in the putamen or globus pallidus.

(7) Dysarthria may result without any pyramidal involvement of genu fibres, and with intact cranial nuclei, from hypertonicity of the musculature concerned.

(8) Tremor is due more particularly to failure of function of the lenticulo-rubrospinal system.

(9) Hypertonicity or rigidity of the musculature, due to defect of the "inhibitory" action of the corpus striatum, is possibly associated with impairment of impulses from that body via the optic thalamus to the cerebral cortex.

APPENDIX.

Cases 1 and 2. Sir WILLIAM GOWERS, *Review of Neurology and Psychiatry*, 1906, vol. iv, p. 249.

Case 3. ORMEROD, *St. Bartholomew's Hospital Reports*, 1890, vol. xxvi, p. 57.

Cases 4, 5, and 6 (abridged). HOMÉN, *Archiv für Psychiatrie*, 1892, vol. xxiv, p. 191.

Case 1.—The patient was a boy, Sydney M., aged 10, who was admitted to the National Hospital for the Paralysed and Epileptic, on October 5, 1886. His father's brother is said to have suffered from a similar affection at the age of 16, and to have recovered after an illness lasting twelve months; a sister of his father also had "St. Vitus's Dance" at the age of 16, which lasted three months; two children of another sister also apparently suffered from some form of chorea and recovered. The patient was the eighth of sixteen children, of whom eleven were dead, one from consumption, the others, it was said, from bronchitis; his eldest brother was in the National Hospital six or seven years before, and died from some form of paralysis at the age of 15. The patient had never suffered from rheumatism. His symptoms began three months before admission, without any exciting cause. Clumsiness with his knife and fork first attracted attention, and the awkwardness in moving the hands gradually increased; spontaneous movement developed and affected the legs as well as the arms.

On admission he was found well nourished. His heart was normal. Constant, slowly changing movements in the limbs and arms at once attracted attention. A contraction of the zygomatic muscles caused a continuous smile, now greater on one side, now on the other. The mouth was usually wide open and the tongue retracted, but sometimes, by an effort, he could slowly protrude it. The open mouth was due to spasm in the depressors of the lower jaw. If told to shut his mouth he pressed the lower jaw up with his hand beneath the chin, and after a moment or two the spasm seemed to give way, and he closed the mouth easily, but in about a minute the spasm came on again and lowered the jaw. The strong retraction of the tongue interfered much with swallowing, because the tongue was pressed up against the hard palate; liquids taken into the mouth ran out again, unless the jaw were raised up; as the jaw began to descend again he was able to flatten his tongue sufficiently to allow the liquid to pass into his throat, but the tongue immediately resumed its rigid position. This process had to be repeated with each mouthful. He seldom tried to speak, but occasionally managed to utter a sentence which could be understood, especially in the morning. The spasm was always less after sleep, and worse as the day went on. He almost constantly made a low whining sound.

The movements of the eyes were normal, but at times the balls were rolled upwards. There was much spasm in the neck muscles, especially at the back, so that the head was almost constantly bent backwards; there was also strong spasm in the sternomastoids. Occasionally, however, when he sat up in bed,

his back and neck were arched forwards so that his head was between his knees.

Both arms presented slowly changing tonic spasm, greater in the left. The forearms were usually pronated; the fingers half flexed at all joints, and the thumb also flexed. From time to time the spasm increased, and then the elbows became strongly extended, the arms adducted at the shoulder. Voluntary movement was interfered with by the spasm to a less extent than might be anticipated; he could take hold of any object with a little difficulty. At times the spasm changed so that the fingers were spasmodically extended; occasionally they were spread out and moved irregularly in a manner resembling athetosis, now and then more quickly, but the constant tonic spasm prevented any actual resemblance to ordinary chorea. It was always increased by an attempt at voluntary movement, even when this could be effected.

In the legs there was similar spasm, also a little greater on the left side. The left foot was in constant strong extension at the ankle, and inverted; the spasm could not be completely overcome by passive force. It varied less than in the arms, but occasionally passed off entirely for a short time. The right foot presented very little spasm, but at times the leg was extended at the hip and knee by spasm, which came on gradually, and slowly passed away. At the hips the spasm occasionally changed to flexion, and the leg, still extended, became flexed on the trunk at the angle of about 60° . The boy was able to walk; the spasm in the left foot generally prevented the left heel from reaching the ground, but now and then relaxation of the calf muscles permitted him to walk naturally. The abdomen was generally retracted by spasm in the abdominal muscles, distinctly greater on the left side.

When the body was spasmodically bent forwards the spine presented one long curve, with a slight lateral deviation in consequence of the stronger action of the muscles on the left side. The knee-jerk could be obtained on each side, but was slight, apparently from the interference of the spasm. There was no foot-clonus. The plantar reflex was slight, the cremasteric active; no abdominal reflex could be elicited. Mechanical irritability of the nerves was repeatedly searched for in the limbs, but could not be found. Sensation was everywhere normal. He complained of some pain in the dorsum of the left foot. His optic discs were normal. His mind seemed unaffected. When the spasm in the tongue prevented his speaking he would write down the word he wanted to say, and evidently understood everything that was said to him. His urine was normal, and so, at first, was his temperature. When he was asleep the spasm passed away entirely, except in the calf muscles of the left leg; the mouth was closed.

During the first few days after admission, a distinct improvement occurred, but after the first week he became rapidly worse. His temperature rose to 100° and 101° F. The spasm had the same character but was greater, and became as severe on the right side as on the left. He ceased to speak intelligibly and became drowsy, and began to pass his urine and stools into the bed.

On October 16 attacks of spasmodic difficulty of breathing came on.

When lying moderately quiet, with the usual spasm of the arms and hands, this would suddenly increase; the mouth opened so widely that the jaw seemed subluxated, and went back with a snap when the mouth closed. As the jaw descended the breathing became quicker, and it was seen that the tongue seemed to be drawn up almost into the throat, so as to impede the breathing, until relieved by drawing the tongue forward and forcibly closing the jaw. During the attack the face was flushed but not livid. Such an attack, lasting half a minute, would recur every four or five minutes. His temperature rose to 101.6° F. and his pulse to 168. The attacks ceased on the application of a spinal ice-bag. Next day he was much quieter, the pulse fell, but the temperature rose to 102.6° F. In the evening the spasms became very violent.

For the next fortnight the condition continued nearly the same, in spite of varied treatment. The temperature continued between 100° and 102° F. and he rapidly lost flesh. Severe paroxysms occurred, in which his respirations were 60 to 80 a minute. The general spasm continued the same in general character, but that in the hands became very uniform. Both were generally strongly flexed at the wrist, the fingers semiflexed, but not forced into the palm, the thumb adducted, the forearm supinated to its full degree, so that the back of the hand was downwards. The face presented little spasm, except during the paroxysmal increase, when his features were distorted. These attacks did not seem to involve the legs, but the extreme extension of the feet continued. The spasm no longer ceased during sleep, but continued much as when he was awake; it seemed to cause little suffering.

A month after admission some improvement occurred: he became able to speak a little. The temperature was generally about 100° F. Emaciation continued; the muscles wasted, but presented no change of electrical or mechanical excitability. In the middle of November there was again an increase in the spasm. The feet were strongly extended at the ankles and the toes were strongly flexed. The spasm of the trunk was still flexor; the body bent forwards, and the thighs flexed at the hip, raising the legs off the bed, so that the patient seemed balanced on the gluteal region. But after two weeks the spasm again lessened, and such flexion of the trunk became rare, but the plantar flexion of the feet and toes increased, so that the sole became arched. The spasm in the arms continued, but the flexion of the left wrist became less than that of the right. During November the temperature varied, sometimes normal for a day or two, then rising to 102°, 103° or 104° F. The wasting steadily increased, so that the child was reduced "almost to a skeleton," although a fair amount of nourishment was taken. During the first fortnight of December the spasm was definitely less, and the temperature was lower, varying from a little below to a little above normal. Occasionally he would talk a little. On December 17 his cheeks and supramaxillary regions were found to be swollen and crepitated on pressure, evidently from air in the cellular tissue. This condition spread down the left side of the neck to the left axilla and left side of the chest, but rapidly lessened in the next few days. The evening temperature was generally 100° or 101° F. The boy became weaker,

ceased to swallow, mucus accumulated in the chest. On December 22 the temperature rose to 104° F., and he died eleven weeks after admission and about six months after the commencement of the symptoms. Throughout, his heart presented no murmur and the urine no albumen. The position of the legs and arms produced by the spasm during life continued after death.

A careful *post-mortem* examination was made, and a thorough naked-eye examination of the brain, spinal cord, and membranes revealed nothing abnormal. The heart was healthy. The cellular tissue of the anterior mediastinum contained air, which extended in front of the trachea and down to the subpleural tissue of the left lung near its root, whence it had evidently escaped. The liver was noted to be "firm, hard, lobular, light in colour, not greasy, and not staining with iodine." (It was evidently cirrhotic, although the significance of this was not realized at the time.) There had been no jaundice.

Portions of the cortex of the brain, of the spinal cord, peripheral nerves and muscles, were hardened and examined microscopically by Dr. Wilson, but no deviation from the normal could be discovered.

Case 2.—Two years later, August 29, 1888, the boy's sister, Charlotte M., aged 15, was admitted, because for nine months she had been restless and lethargic, with some thickness of speech and tendency for saliva to flow from the mouth. At the onset the catamenia, established for eighteen months, had ceased. She was a heavy-looking girl, with mouth generally open and lower lip hanging down, easily excited to laughter. The tongue was rather large, and when protruded had a slight tremulous movement. There was nothing abnormal in the throat except some congestion. She was able to walk well; the knee-jerks were normal; there was no foot-clonus; the optic discs were normal, and no other symptoms were found. At the end of six weeks she was sent to the country branch. But six weeks later "choreic movements" commenced in the right leg, and extended to the other leg and to both arms in a fortnight. She was readmitted on January 2, 1889. The movements increased during the month before admission, and for a few days the legs had been drawn up, flexed at the hip and knee, while her arms were extended and raised above her head. Lying thus there was constant regular movement of the feet, the heels resting on the bed and the toes sharply depressed, and then raised; at the knees and hips there were also slight flexor and extensor movements, moving the heels up and down the bed for an inch or two. Similar rhythmical movements occurred in the arms at the elbows. The trunk muscles and those of the neck and head were free, and the face was still. The tongue now presented no tremor or spasm, and could be voluntarily protruded.

The movements varied in degree, and could be occasionally stopped for a few seconds by voluntary effort. There was no tenderness of the muscles or wasting. Passive movements caused some pain, especially attempts to extend the legs. The knee-jerks could not be obtained (perhaps from the spasm); there was no foot-clonus.

No derangement could be found in any cranial nerve, pupils, eye-move-

ments, or optic discs. The heart was healthy. The urine contained one-sixth albumen (casts are not mentioned). The temperature was raised, and during the first three weeks it frequently reached in the evening 103° or 104° F. She steadily lost flesh and became thinner and more feeble, the movements continued, varying much in degree. At times the forearms were brought in front of the chest, and moved rapidly in flexion and extension.

The only medicine which had a marked effect on the movement was the hydrobromate of hyoscyne, but toxic effects prevented its continuance. On the evening of January 23 her temperature was 106.2° F. (verified by several thermometers), reduced to 100° by cold sponging. There was no delirium or headache, the pulse was 180 and respiration 68, although no morbid sign was presented by the lungs. The patient became much more excited, and, apparently in consequence of this, the movements became less violent. The heart-sounds continued normal, but bronchitic râles appeared. The albuminuria continued. Twice again the temperature rose to 106° F. Evacuations were passed into the bed. She died on January 30, the temperature rising just before death to 108.4° F.

Post-mortem examination revealed no morbid appearance in the membranes of the brain; no sign of tubercle could be discerned in them. The white substance of the hemispheres was studded with minute "pits," the size of a pin's head (the significance of which is probably small). No other morbid state could be discovered in the brain. The spinal dura mater was, in places, adherent to the bone, but was not thickened, and presented no other morbid appearance. In the lower dorsal region there was a small extravasation outside the dura mater, but there was no morbid appearance on its inner surface. The spinal cord and sections of this in all parts appeared perfectly normal to the naked eye. The heart was healthy. No sign of tubercle could be found anywhere. In the lungs there was very slight hypostatic congestion.

The liver, of normal size, presented the typical appearance of cirrhosis. Strands of connective tissue enclosed yellow lobules of various sizes rising above the level of the section. The tint was found to be due to fatty and granular degeneration of the cells. The condition of the liver led to careful inquiry regarding alcohol, but it was found she had never taken it. There is no record of a microscopical examination.

Case 3.—Walter William S., aged 10. Admitted to Luke Ward, St. Bartholomew's Hospital, under care of Dr. Gee, September 20, 1889. Transferred to Casualty Ward, October 22, 1889. Died January 21, 1890.

Note on admission.—Three or four months ago right arm and hand noticed to be weak, and fingers to be kept in cramped position. Speech affected soon after arm; could not pronounce his words intelligibly. Speech got a good deal worse about a month ago; has since been scarcely able to speak at all. Not walked quite naturally for two or three months, but this has got much worse during the last fortnight. No difference noticed in the two legs. For about the same time the left arm and hand have "not been right." No trouble with

micturition or defæcation. Some drawing of the face has been noticed from the beginning, but only occasionally, and usually to the left. No squint. Has seemed silly (laughing unnecessarily, &c.) for a month or two. Never had fits.

For about a month has had some difficulty in swallowing; food does not come back through nose, but returns through mouth. Lately saliva has run from mouth. During three or four months some bleeding from ears and mouth; never pus; never headache or giddiness. No vomiting.

Always fairly healthy; got on fairly at school, though never very sharp (in second standard).

Three other children in family—these died young; one with "rheumatism of the heart," two with whooping-cough and fits.

Mother dead; had one or two miscarriages. No family history of consumption or insanity. Maternal uncle subject to fits. A further note, October 31, states: He comes of a neurotic stock. His father frequently weeps; his aunt, is said to have had the shaking palsy, and to have recovered from it after eighteen months.

Present condition.—Has rather an idiotic look.

Eyes.—Pupils widely dilated, act well to light and accommodation. Movement of eyeballs good in every direction; no squint or nystagmus. Sight appears good; optic discs natural.

Ears.—Some dried blood in each; no deafness, perosseous or otherwise.

Face.—No very manifest paralysis. Eyes can be closed tightly. On laughing both sides of face move well. Mouth is kept open; it is sometimes drawn a little to right, sometimes to left. He can open it widely; the jaw muscles can be felt to contract well on closing it.

Tongue.—Furred; protrudes it a little way only beyond lips; irregular movements as he does so.

No power of *speech*; cannot say "yes" or "no," but makes the same sound whatever he tries to say.

Throat.—Natural; normal movement of soft palate.

Arms.—No actual paralysis of either arm. Right thumb is kept more or less flexed into palm; is unable to close fist without first drawing out thumb with other hand. Grasp of right weaker than left. Slight rigidity sometimes at wrist and elbow; no increased reflexes. No manifest wasting anywhere, but perhaps a little about thenar eminence. All movements of hands and arms performed fairly, but he cannot pick up pin with right hand. No anæsthesia.

Legs.—Perhaps some rigidity at knees; knee-jerks marked, + right; no ankle-clonus.

Gait.—Rather uncertain and stiff; stands well with feet together and eyes shut.

Pulse 80, good strength. *Respiration* quiet. *Temperature* normal.

Chest.—Heart and lungs normal. *Abdomen* normal; skin reflexes marked.

Spine.—No tenderness or curvature of spine.

Mental condition is perfectly clear; does everything he is told at once.

September 21.—*Urine*, alkaline, 1.014; no albumen or sugar.

September 22.—As to swallowing, nothing very remarkable has been noticed; he eats and swallows mince without any difficulty; he moves his lips well. In drinking he has rather more difficulty, letting the fluid come back from mouth into cup; chokes a little sometimes. Feeds himself quite well; spoon held in right hand, but very awkwardly.

September 23.—Electrical reactions quite natural.

September 24.—Right tympanic membrane seen; looks natural.

September 25.—He can write his name (a specimen appears in the original notes). Nothing can be said about it except that it is clumsy, the letters of different sizes and the upstrokes a little shaky; sometimes will mention a letter pointed out to him, but never pronounces them distinctly; evidently knows the letter well. Sometimes asks for what he wants.

September 26.—Spoke distinctly this morning; referring to his medicine, said "That is water"; but when asked to say anything does not seem able to.

September 29.—Always talks best first thing in the morning.

October 3.—Last night left side of face was much drawn down. Can protrude tongue better. Cannot use hands at all, but is willing to try.

October 11.—Is now frequently suffering severe paroxysms of pain in the left hand. The contractions are then more rigid.

October 15.—Every day has attacks of pain in left hand, and shrieks; lower part of face (not upper) drawn to left. Seems more placid when asleep, and can draw down the mouth at will. Left hand continues flexed and in a condition like tetany, even when asleep. Can talk plainly sometimes.

October 22.—Very noisy and quite a nuisance (had to be transferred to Casualty). Behaves in an idiotic manner. Is able to relax his facial muscles at will.

October 31.—His condition is investigated and described as follows: Thin and emaciated. Pupils dilated; fundi natural. Mouth drawn to left; left side of nose drawn down, and left nostril dilated, but these distortions seem to be voluntary. Can protrude tongue but not at once, and creates some trouble over it. Is unable to talk. Does not seem to be paralysed at all. Left arm is kept contracted at elbow; straightened when he likes. Left wrist and fingers flexed; can also be straightened. Right arm and hand fairly normal, but some approximation of thumb to palm. Prefers to lie with his thighs and knees flexed and feet *en griffe*. But on the application of the needle will put every joint in its ordinary position. Muscles react well to faradism; no R. D. Can walk when he chooses. When he falls about he bruises himself, but not seriously.

November 3.—His temperature, hitherto normal, rises (*vide* chart, fig. 8).

November 4.—Last night had a hot bath; with a view of seeing what he really could do, he was allowed to go under the water. He seemed to realize his position, but made no effort to help himself; swallowed enough warm water to make him sick. Sweated much after the warm bath. Thirsty and feverish this morning. Pain in belly over region of liver.

November 5.—Bit his lower lip slightly. Tongue dry and coated with blood.

November 7.—Dr. Gee can find no signs of local disease to explain the fever. Ophthalmic examination gave no results. After examination he lay and yelled lustily. 4 p.m. sweating profusely. Looks as idiotic as ever.

November 8.—Profuse sweats. Heart-beats 226. Respiration 40. Temperature fluctuates, *vide* chart (rose to 103.6° F. to-day). Takes food well.

November 9.—Improvement. Anæsthetic given and splints applied to straighten the legs; respiration became slower and more regular under the anæsthetic.

November 10.—Left arm much better, uses it volitionally, but right hand appears to be gradually taking on the same characteristics as left; the thumb is adducted and the fingers are beginning to be flexed. He likes the splints. Distinctly said "No" in answer to a question from the house physician. Has paraldehyde to procure quiet nights.

November 13.—Bed-sore appeared on sacrum since yesterday (the splint has been removed).

November 14.—More feverish again. Much flexion of right little toe. Less flexion of legs. Howls vehemently.

November 16.—Ories when he wants anything, but does not speak. Swallows everything that is given him, but does not masticate. Is quite anæsthetic over the bed-sore.

November 18.—Temperature reached 105° F. to-day. Another bed-sore, character like the last. Urine very offensive, alkaline and phosphatic.

November 21.—Face bluish. Still lies drawn up. Never asks for anything. Still yells.

November 22.—Fever abated (*vide* chart); and seems better, excepting the bed-sore, which is worse. Marked spasm of right facial muscles when he attempts to speak.

November 23.—Less rigidity of arms, legs still contracted; looks more cheerful. The improvement seems to have been maintained till December 7, when the constant yelling recommenced. Still lies in fantastic attitude. Understands, but cannot formulate words.

December 10.—Howls dismally about sixteen out of the twenty-four hours. Takes food well, can appreciate when his mealtimes come, but does not speak. Fundus of eyes rather hazy. Bed-sore better. As to the contractions, knees flexed, feet extended. Face now drawn to right, constant movement of right facial muscles.

December 13.—Hard places on lower lip and left cheek, apparently where rubbed by the teeth.

December 30.—Temperature, which has lately been nearly normal, begins to mount again in an irregular fashion (*vide* chart).

January 1, 1890.—His condition is again described thus: He has no appreciation of time or season now; the only thing he can do, and that not humanly, is to devour food ravenously when put into his mouth; he does not chew it,

and is therefore fed on slops. His posture is as follows: Knees drawn up one on either side of chin, so that thighs are flexed on abdomen, and legs on thighs. Feet extended and toes flexed. Left arm flexed to a right angle at elbow, forearm across chest. Left hand flexed at wrist, thumb adducted, and finger adducted and flexed. Right arm generally extended by side, forearms pronated as far as possible; thumb adducted, fingers adducted and a little flexed. In this position he lies, usually howling dismally, so that a half-grain of morphia is given daily. The perverted action of his muscles is intensified, and on the slightest forcible action clonic spasms can be produced. His right eye works now, and the right side of his face. His mouth is not sore, but he has neither the volition nor the power to put out his tongue. He passes everything under him. He sweats profusely. Fundus of eyes natural. Electric reactions natural.

January 15.—The fever, which had abated somewhat since the 4th, is again increasing. Breathes very rapidly. Does not howl so much, sleep induced by morphia. But is in a most deplorable condition; passing everything under him, and lying like a log unless turned over. Bed-sore healed.

January 19.—Much worse, breathes very infrequently, usually four times to the minute.

January 21.—Died.

I made the *post-mortem* the day after his death. The following is a record from the *post-mortem* book:—

External appearances.—Extreme emaciation. Bed-sores on sacrum, trochanter and right elbow. Legs tightly flexed upon his hips, and hips on thighs; they could not be straightened out.

Head.—Cranial bones very thin. Dura mater and sinuses normal. Arachnoid and pia mater rather watery-looking, otherwise normal. Arteries normal at the base. Brain: convolutions perfectly normal in appearance and to touch. Spinal cord normal to naked eye.

The brain and cord were put in spirit and water till next day.

Eye and ear.—Not examined.

Neck.—Not examined.

Chest.—Lungs dirty and flabby-looking, and smelling badly, but no definite disease.

Heart.—Normal.

Aorta and vessels.—Normal.

Abdomen.—Peritoneum normal. Stomach normal. Intestines discoloured. Liver in an extreme state of cirrhosis, weight 16 oz. In size, uniformly small. Surface covered with small rounded elevations. Section firm, and showing bands of connective tissue, enclosing degenerating lobules. Some few of these lobules were yellowish, and so disintegrated that they could be pressed out of the section. General colour of the organ a sort of pinkish-brown.

It was sent to the Museum as a specimen of typical hob-nailed liver in a child.

(In order to meet the wishes of the friends, the examination was to a

certain degree limited, so that the nerves of the limbs were not removed, nor the joints opened.)

Vertical sections were made through the brain next day. In a section at the level of the optic commissure (practically equivalent to the frontal section of Pitres) a small patch of softening was noticed, having the shape and position indicated in the diagram (see p. 310)—i.e., involving the outer layer of the left lenticular nucleus. On a section about $1\frac{1}{2}$ in. farther forward (pediculo-frontal) and on the next section behind (viz., through anterior border of pons = parietal section), this softened patch could no longer be seen. Dr. Gee examined the sections after they had been two days in Müller's fluid. He noticed another similar but smaller streak, symmetrically placed upon the right side. He pointed out that these alone could not explain the whole of the symptoms.

The brain, pons, medulla, and cord were hardened in Müller's fluid, and then further examined. The streak of disease by the left lenticular nucleus was then found to extend backwards and forwards for about an inch, tailing off and gradually disappearing within these limits, but preserving the same position in relation to the adjacent parts of the brain. Thus it formed a small flat area, covering a considerable part of the external aspect of the nucleus, between this and the claustrum. The tract of disease on the right side was in every way symmetrical to the left, except that it was smaller in extent. Microscopically these tracts of disease were found to consist of closely packed lymphoid cells, in which a few vessels ran. They were, I presume, inflammatory.

In the upper part of the pons were some tiny patches, apparently of softening, placed as follows:—

(1) In a section just below the superficial origin of the fourth nerve were two narrow patches, one on each side of the mesial raphe about $\frac{1}{4}$ in. from it. They were in the dorsal part of the transverse fibres of the pons, lying in the direction of these transverse fibres, and measuring at most $\frac{1}{8}$ in. in length.

(2) In a section about half-way between the superficial origins of the fourth and fifth nerves were two little patches corresponding in position to those just described, but smaller; and two other points, the size of pin-heads, lying still more dorsally—i.e., in the fillet.

Microscopical examination was made of many parts of the motor area of the cortex cerebri and of the cortex cerebelli. I could not make out any disease here. The spinal cord also was perfectly normal; there was no trace of descending degeneration to account for the contractures. In the liver was found what was expected from the naked-eye appearances—viz., large bands of connective tissue occupying the periphery of the lobules. In the sections I have, the cells of the lobules are less degenerate than I should have expected. Moreover, amid the connective tissue growth bile-ducts are very numerous and very prominent objects.

Case 4.—Alfred K. was born on December 1, 1866, and was the third member of the family. During his boyhood he had been perfectly healthy, and

not suffered in any way. At the age of 20 he was working as a carpenter. Not long thereafter, in the spring of 1887, he began to suffer from headache and general listlessness, and about the same time his mother noticed that he seemed to become more "simple," and in a general way to "fail" (expression of his mother). At the same time his memory became impaired, but at this time no other symptoms were present.

After about a year of this or rather less, during which time the symptoms were slowly increasing, the patient began to walk in an irregular and uncertain fashion. He also complained of occasional pains in his legs.

At the beginning of 1888, that is to say, about a year after the onset of the illness, he began to have difficulty in articulation. At the same time, or perhaps a little later, a certain stiffness of the whole body was noticed, especially in the lower extremities, which began to contract slightly at the knees and hips. Slight but definite tremor made its appearance in the arms and hands, and gradually increased. All these symptoms gradually became more intense, with the result that the patient became more and more helpless. Occasionally there was vomiting. From December, 1888, the patient was bedridden, and unable to feed himself.

On May 6, 1889, he came under the observation of Professor Homén, who made the following examination:—

The patient is rather small and delicate-looking, but his nutrition is good. The expression of his face is childish, stupid and half idiotic, and somewhat staring. Speaking generally, he seems to take in what goes on round about him, answers simple questions slowly, as if he were thinking about them, but sometimes he does not respond at all. Speech is slurring and difficult, and restricted to a few words or to a short sentence; on the other hand, he does not miss his letters or make mistakes in his words. Movement of the tongue appears somewhat difficult, but there is no fibrillation. The pupils are of medium size and react to light, although a little slowly. Vision is normal, and the other organs of special sense are also normal.

The customary attitude of the patient is as follows:—

He usually lies on his side with his head drawn a little back, though the neck muscles are not much contracted. When he sits up his head usually moves to and fro in a fine tremor. His mouth is often held open, and there are occasionally slight tremors of the lower jaw. Both arms, especially the left, are somewhat flexed, and cannot be straightened beyond an angle of 150° . At the wrist the left hand can be drawn into a line with the forearm, but cannot be dorsally flexed; the first and second phalanges are flexed to a right angle, the third phalanx is in slight dorsal flexion; the forefinger is not so flexed as the others. It is almost impossible to straighten the other fingers. The thumb is contracted, and its movements are very imperfect. The right hand and its fingers is much less contracted and more movable. Almost always a slight slow tremor of the hand is present, mostly from side to side, but occasionally also rotatory. The forearms when they are held free also show a tremor of alternating flexion and extension.

The lower extremities are also contracted, especially at the knee and hip. The knee cannot be extended beyond 150° . Both legs show very definite tremors, especially when the patient tries to straighten them. These consist of alternating movements of the knees and toes.

The musculature is slightly atrophic. The cutaneous reflexes are "weak"; the tendon reflexes cannot be tested well, because of the contractures. There is no obvious disturbance of sensibility and the electrical reactions of the nerves and muscles are normal. The left hand is so tightly closed that it cannot be opened, but the power of the right grasp is fifteen on the dynamometer. During this test a wide, coarse tremor becomes manifest.

During his stay in the hospital the patient's condition gradually became worse in every respect. His perceptive powers seemed to become more feeble, and during the last weeks he never spoke at all, more apparently from failure of perception than from inability to articulate, since even to the end he could occasionally articulate a few words correctly. As a rule the sounds that escaped from him were more or less unintelligible.

The contractures were intensified, but the tremor became rather less; towards the end it came in attacks, which spread over the whole body and lasted from five to ten minutes. Saliva escaped from the constantly open mouth. During the last few weeks of the patient's life, tonic and clonic attacks of cramp lasting about a minute were sometimes noticed. During his stay in the hospital he had steadily emaciated, and a few slight bed-sores made their appearance. On September 1, 1890, his temperature began to rise, and his tonsils became inflamed and swollen. He gradually sank, and on the evening of September 13, 1890, he died, being scarcely 24 years old.

The *post-mortem* was held the next day, and of the long description which the author gives, the following are the essential points:—

The contractures were extreme. It was quite impossible to straighten the arms and legs. The cranium was thickened. The dura mater was slightly thickened also; the pia mater was somewhat oedematous, and in one or two places slightly adherent to the cortex underneath.

The weight of the brain (including the cerebellum and the medulla) was 1,060 gm. The convolutions of the frontal lobes appeared slightly atrophic, but both halves of the brain were symmetrical, and the convolutional pattern was normal. On transverse section the grey matter of the cortex, especially of the frontal lobes, seemed a little thin. By a section across the basal ganglia it was seen that the middle division of the lenticular nucleus on both sides was softened and discoloured over an area about 1 cm. long and broad. The other basal ganglia and the internal capsule were perfectly normal.

There were slight sclerotic patches in the aorta. The liver weighed 1,160 gm., was of firm consistence, and had a knotty, granular surface. Its capsule was slightly thickened in places. On transverse section it was seen to be typically cirrhotic, with numerous nodules of liver-tissue, separated by abundant, small, grey-white bands of connective tissue formation.

The spleen was of normal consistence and its capsule smooth. It was not obviously enlarged.

MICROSCOPICAL EXAMINATION.

Brain.—Nowhere was there any obvious diminution of the medullated fibres, although in a few places in the frontal lobes there might be slight diminution, but it was nothing like so marked as in a case of general paralysis. Where it was present it concerned chiefly the tangential fibres and the supra-radiary network. Over the frontal lobes the pia mater was thickened in places and a little infiltrated with round cells. The neuroglia also appeared a little thickened, especially in the tangential layer, but in any case the changes were not nearly so marked as in general paralysis.

The blood-vessels were distended with blood, and in some places appeared to be widened. The walls of the vessels and of the smallest capillaries were here and there thickened and had a sclerotic or hyaline appearance. In the walls of the vessels were small collections of fine fatty granules, which sometimes bulged into the lumen of the vessel. Very occasionally there were found a few round cells in the adventitial lymph-sheaths. Occasionally also in the blood-vessels, or rather in the perivascular spaces, were yellow-coloured refractile pigment-granules. There were perhaps slight changes in the large pyramidal cells of the cortex; some of them were normal, others seemed small and shrunken or sclerosed, with diminution of their processes and with pigmentary degeneration.

In the vessels which leave the middle cerebral artery to supply the basal ganglia the changes already described were more marked than elsewhere. In one or two places there were very small cellular masses, which looked like thrombi which were commencing to organize.

The pons and the medulla were normal.

Spinal cord.—The spinal cord, examined at various levels, was perfectly normal.

Nerves.—The nerves showed no changes that could be considered of any significance.

Muscles.—The muscles appeared normal, perhaps here and there a little atrophic, but without further degenerative changes.

Liver.—The nodules of cirrhotic tissue contained as a rule from three to five lobules, but sometimes more, and occasionally only one. In the strands of cirrhotic tissue were numerous bile-ducts. Occasionally also there were very fine strands of connective tissue between the columns of liver-cells and sometimes also between individual cells. In these lobules the liver-cells were often quite normal, but others showed fatty degeneration. The whole liver picture bore a marked resemblance to that of "cirrhosis hypertrophica adiposa."

Case 5.—Wilhelm K. was born on August 8, 1870. Up to the age of 3 he suffered from slight attacks, the nature of which is not very definite; apparently they were like *petit mal*. He developed perfectly normally, and at the age of 12 was "fat and well." In the autumn of 1882, for no apparent reason, he began to suffer from slight attacks of giddiness. At the same time he

complained of headache, of pains in his limbs, and of a general feeling of tiredness. About the same time his understanding and his memory seemed to fail. Almost from the outset it was noticed that his gait was somewhat uncertain.

After these symptoms had continued for about a year it was noticed that the patient's speech was becoming defective, and at about the same time his arms became stiff, so that he could not use them properly. Tremor made its appearance in the upper extremities, while the legs also began to get stiff. As a result the latter soon became flexed at the knees and hips.

All these symptoms steadily increased, so that after three or four years the patient became bedridden and had to be fed by others. His speech was limited to a very great extent; it was only rarely that he spoke at all, and then with great difficulty. Saliva constantly escaped from his half-open mouth. Occasionally he had attacks of vomiting.

On December 11, 1888, he was taken to the hospital to be under the care of Professor Homén. It was then remarked that his general look and appearance suggested complete dementia. He did not appear to understand what was said to him, or to pay much attention to what was going on around him. He never spoke at all, but occasionally unintelligible sounds escaped from him; and yet, if he were disturbed or aroused, he could articulate a few words well enough, and even make use of short phrases, of course with difficulty.

The pupils were of medium size and reacted alike slowly to light. Contractures were very pronounced, so much so that the knees were flexed over the abdomen. The arms, too, were flexed. It was possible, however, to straighten the limbs by passive movement, though not to their full extent. As a result of the contractures and of the patient's mental condition he was reduced to utter helplessness. Tremor was almost constantly observable in the hands and arms, occasionally also in the head and in the legs. The musculature was slightly atrophic, and the patient generally much emaciated. The cutaneous reflexes were "weak." The tendon reflexes could not be tested because of the contractures. The patient's condition steadily deteriorated and he died on October 17, 1889, being then 19 years old.

The *post-mortem* examination was held the next day. The contractures of the limbs, more especially of the legs, were extreme. There were bed-sores on the trochanters and elsewhere.

The cranium was thickened; the dura mater also was somewhat thickened. The pia mater was oedematous and in one or two places adherent to the underlying cortex. The weight of the brain was 1,160 gm.; this included the cerebellum. The cerebellum, pons, and medulla weighed together 130 gm. The convolutions of the brain appeared normal, with the possible exception of very slight atrophy of the frontal and central gyri. On transverse section the cortex was possibly somewhat thin in the frontal and central regions. On horizontal section through the basal ganglia, the optic thalamus, internal capsule, and the caudate nucleus were perfectly normal. On the other hand, in the middle of each lenticular nucleus, and symmetrical on the two sides, was a cavity which began about half a centimetre from the upper surface of the nucleus

and was 3 cm. long. More than half of the lenticular nucleus was completely destroyed in breadth, and the cavity which was left contained some serous fluid. The cavity extended to the posterior and inferior end of the nucleus. Round the cavity the tissues were softened for an extent of several millimetres, otherwise the brain seemed perfectly normal.

There were a few sclerotic patches in the aorta.

The spleen was 17 cm. long by 11 cm. broad, and of firm consistence.

The liver was $21\frac{1}{2}$ cm. long, 13 cm. broad, $7\frac{1}{2}$ cm. high. Its surface was markedly cirrhotic. The capsule was in one or two places thickened. On section, the liver was seen to be composed of nodules about the size of lentils or larger, surrounded by strands of connective tissue.

MICROSCOPICAL EXAMINATION.

The fine fibres of the cortex, especially in the tangential and supraradiary layers, were slightly diminished, and the neuroglia was slightly thickened. In the blood-vessels there were here and there small localized endarteritic changes, consisting of minute, granular, more or less homogeneous masses, which often bulged into the lumen of the vessel. These masses lay between the intima and the fenestrated membrane, and occasionally seemed to break through the latter. The changes were most commonly seen in the perforating arteries coming off the middle cerebral artery.

The tissue round the cavity in the lenticular nucleus was softened and crumbling, and infiltrated with cells, but under the microscope no further changes could be seen in the basal ganglia or internal capsule.

The pons, medulla and spinal cord were entirely normal.

Sections of the liver, as in the first case, showed a mixed type of cirrhosis, which was partly multilobular, partly interlobular, partly intralobular. There was marked fatty degeneration of much of the liver-tissue; in the cirrhotic tissue bile-ducts were abundant.

Case 6.—Anna K., the eldest member of the family, was born on July 6, 1862. Her mental and physical development was perfectly good. In her 20th year, towards the end of 1882, exactly the same symptoms as in the case of her brothers made their appearance. She complained of giddiness, headache, general tiredness, and loss of appetite, and at the same time her memory became less good. After about six months or more it was noticed that her walking was a little irregular; at the same time she complained of occasional pains in her legs.

At the age of 22 the muscles began to get stiff and not long after contractures set in at knees, hips and elbows. Articulation became more and more difficult. At this time or a little later tremor appeared, most marked in the arms and hands. All these symptoms steadily increased, so that the patient became helpless and bedridden. She had considerable difficulty in swallowing, and the saliva escaped from her open mouth.

The patient entered the hospital on August 29, 1888. She was completely

helpless, looked demented, lay apathetic in bed, did not speak at all, and paid no attention to what was going on around her. Occasionally she gave vent to a few inarticulate sounds, and yet sometimes she could articulate a few words distinctly, though with difficulty. She died from inflammation of the lungs on October 19, 1888, at the age of 26.

The *post-mortem* examination was held the next day.

The cranium was thickened, as was the dura mater. The pia mater was slightly adherent in one or two places to the cortex underneath.

The frontal convolutions appeared a little shrunken. On section, both lenticular nuclei were softened in their central part and coloured a patchy grey-yellow. The brain with the cerebellum and medulla weighed 1,130 grm.

There were a few sclerotic patches in the aorta.

The spleen measured 12×7 cm. The liver measured $25 \times 14 \times 8$ cm.; it was obviously cirrhotic, and on section the nodules of liver-tissue were seen to be about the size of hazel-nuts, though they varied considerably. They were surrounded by firm, grey, fibrous bands.

Microscopical examination of the basal ganglia showed that in the degenerated area of the lenticular nucleus on each side there was commencing disintegration, with degeneration of nerve-cells and fibres.

In the blood-vessels there were a few circumscribed endarteritic changes. Here and there in the degenerated area, slight small-cell infiltration was noticed.

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ADDENDUM.

WITHIN a few days of the publication of this monograph my attention has been drawn to a paper, by Völsch, on "Pseudosclerosis" (*Deutsche Zeitschr. f. Nervenheilk.*, September, 1911, Bd. xlii, S. 335), in which that author describes a case diagnosed, not without reserve, as pseudosclerosis, which in many ways resembles progressive lenticular degeneration. The patient was a girl, aged 17, of previous normal development, who for about two years, or rather more, had suffered from rhythmical tremors of the limbs and trunk, occasional paroxysmal attacks of violent tremor, and spastic contractures of the extremities. The mouth was always open; dysarthria and dysphagia were present; the facies was immobile. There was no actual paresis, and sensibility was intact. The plantar reflexes were flexor in type, while the abdominal reflexes were preserved. There was some slight general mental impairment and dulness. The patient died from scarlatina at the age of 17. *Post-mortem*, there was marked atrophic cirrhosis of the liver, which had not been diagnosed during life, and considerable enlargement of the spleen. The brain was hardened and cut in slices, but no abnormality was found. Völsch considers the case to be probably a variety of the pseudosclerosis of Westphal and Strümpell, though he admits it differs in several important particulars.

It will be clear to the reader that a case of this description bears the closest analogies to those here reported, and this being so, it is peculiarly unfortunate that the pathological details are so meagre. There is no account of the direction of the slices into which the brain was cut, an important matter when it is remembered that an atrophic but not disintegrated putamen might not thus be remarked; there is no note of any microscopical investigation of the corpus striatum; the cortex and cord apparently were all that were examined microscopically, and they were found to be normal. Notwithstanding the dearth of information, this case, I believe, comes under the category of those which I have described.

Pseudosclerosis is a nosological conception which has been utilized to include very varying cases, in not a few of which pathological examination has been so restricted as to be valueless. But among

those thus classified there has been at least one other, besides Völsch's case, in which cirrhosis of the liver occurred, complicated, it is true, with diabetes (Fleischer, *Münch. med. Wochenschr.*, 1909, S. 1120). In view of the material collected in the present article, it is desirable that the unsatisfactory and makeshift expression "pseudosclerosis," which was coined for certain cases which were said to resemble disseminated sclerosis clinically, but not pathologically, should be abandoned, and that reinvestigation of the subject should be undertaken.

A CASE OF SUBACUTE COMBINED DEGENERATION OF
THE SPINAL CORD DEMONSTRATING THE NATURE
OF THE AFFERENT IMPULSES IN THE POSTERIOR
COLUMNS.

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APART from the well-known degeneration of the spinal cord in tabes dorsalis, isolated lesions of the posterior columns are distinctly rare. In the following case the destruction of the spinal cord was limited almost entirely to the posterior columns, and the case affords an excellent opportunity for studying the nature of the impulses carried upwards by the fibres of these columns.

The lesion was associated with a condition of grave progressive anæmia in a man, aged 53. At the *post-mortem* examination a granu-
lomatous ulcer of the stomach was discovered, the base of which was gangrenous, and upon microscopical examination was shown to consist of necrosed tissue containing large numbers of long unbranched Gram-positive mycelial threads in addition to numerous micrococci and bacilli. The case is therefore of interest also as bearing upon the relation of grave anæmia and the allied spinal cord changes to infective processes within the alimentary tract.

CLINICAL HISTORY AND CONDITION.

J. K., a boiler-maker, aged 53, was admitted to the London Hospital on November 30, 1910, complaining of loss of the use of his hands and legs:

Except for an attack of small-pox when 19 years old, he had always been in good health. He denied infection with syphilis or gonorrhœa. He had been married for thirty years and had had ten children, of whom nine were alive and well. His wife was healthy, and had had no miscarriages. For the last ten years his wife had left him on account of his drinking habits. There was no history of nervous disease in his family.

His illness began two months before admission and the onset was gradual. The first thing he noticed was that he was beginning to grow pale. Six weeks before admission he gradually began to lose the use of his fingers. They "became awkward," and he found he could not fasten the buttons of his waistcoat. The fingers "seemed dead," and he could not feel anything with them, so that he was unable to hold a cup or anything in his hands. He stated that the hands felt like "boxing gloves," and his fingers appeared to him to be greatly swollen. He complained of a curious sensation in his hands like "electric shocks." Later his legs had become affected so that he could not stand properly. He stated that "his knees went sideways when he stood up." He also complained of stinging sensations in his toes, which appeared to him to be "swollen to the size of flower-pots." He had become gradually weaker and had lost 3 st. in weight during the last three months. He had had no pain at all throughout his illness.

On admission the patient was seen to be very anæmic, the skin was of a deep lemon tint and the mucous membranes were very pale. There was evidence of considerable general wasting. His tongue was clean, but the teeth were carious. There was much retraction of the gums and definite pyorrhœa alveolaris was present. There was no vomiting, and the bowels were open regularly. The abdomen was flaccid, and no tenderness was elicited on palpation. The abdominal organs were normal as far as could be ascertained. There was some emphysema of the lungs and a little bronchitis. The heart was normal, the arteries were somewhat thickened, the blood-pressure was normal. On pricking the finger the blood was seen to be distinctly pale, and on December 2 a blood examination was made with the following result:—

Red blood-cells ...	...	...	1,620,000.
Hæmoglobin ...	...	...	35 per cent.
Colour index ...	...	...	1.1 „
White blood-cells:—			
Polynuclear neutrophiles...	72	„	
Small lymphocytes ...	20.5	„	
Large lymphocytes ...	2.5	„	
Eosinophiles ...	1	„	
Hyaline cells ...	4	„	

The red cells showed very slight rouleaux formation and poikilocytosis was present. One normoblast was seen during the counting of 200 leucocytes.

In spite of treatment the anæmia increased, and on December 23 the blood condition was as follows :—

Red blood-cells...	...	...	1,220,000
Hæmoglobin	...	...	35 per cent.
Index	...	...	1.4 „

Numerous degenerated red cells were seen, and thirty normoblasts were counted among 200 white cells.

The white blood-cells count was :—

Polynuclear neutrophiles	...	...	67 per cent.
Lymphocytes	...	...	17 „
Eosinophiles	...	...	8 „
Hyaline	...	...	8 „

The urine was normal, and from 20 to 56 oz. (from 560 c.c. to 1.5 litres) were passed daily.

The temperature was normal on admission. On December 3 it rose to 101° F., and on December 6 to 102° F. On December 8 it fell to normal and remained subnormal to his death on December 27. His pulse was feeble throughout, and varied in rate between 60 and 90 per minute.

Nervous System.

The most striking changes, however, were found on examination of the nervous system. His intellect was normal, and he answered well to sensory testing until the last few days of his life. He had no headache or fits. The voice was somewhat nasal in character, but the patient had himself noticed no change.

The *cranial nerves* were normal. The pupils reacted well to light and to accommodation. Vision was good. Ophthalmoscopic examination showed the optic discs to be very pale and the vessels small. Just above the left disc was a small hæmorrhage. The movements of the eyes and face were normal. The tongue could be protruded naturally and the palate moved well.

Motor system.—The muscles of the arms and legs were poorly developed, but there was no localized wasting. There was no loss of power, and when lying down he showed considerable vigour in resisting forcible movements of his limbs. The hand-grasps were fair and equal. There was much ataxia of the arms. He could not touch his nose with his eyes shut, nor could he make his forefingers meet under the same conditions. He could not walk alone, and when aided

the gait was extremely ataxic. Romberg's sign was well marked. There was slight stiffness on passively moving his legs.

Reflexes.—The elbow-jerk and wrist-jerk were easily obtained on both sides. Both knee-jerks were present, but ankle-clonus was absent. The response to stimulation of the sole varied. Sometimes no response was obtained, at others the plantar reflex gave a normal response on both sides, but occasionally there appeared a definite extensor movement of the left great toe.

Sensory system.—Painful sensibility was tested by pricking with the point of a pin. There was no loss anywhere; in fact, over the lower limbs there seemed to be a definite hyperæsthesia to painful stimulation. A pin-prick would cause a movement of withdrawal of the whole leg, accompanied by a spasm of the facial muscles and often a cry, the whole response being in excess of what one would have expected from the nature of the stimulus.

Heat and cold could everywhere be distinguished with ease from one another. Stimulation with the hot test-tube over the legs produced a response very similar to that obtained by pin-prick, there being a condition of hyperæsthesia.

Tactile sensibility was normal. Both light touches and pressure could be everywhere appreciated.

The most striking sensory change was the profound loss of the sense of passive position. He was quite unable to tell the position of his fingers, his hand, or his forearm. For example, the patient's eyes were closed, the right wrist was strongly flexed, and the patient was told to put the left hand in a position similar to that of his right. He placed his left hand in an entirely different position, and when he was allowed to open his eyes he was surprised to find his right hand in its strongly flexed position. When the right elbow-joint was strongly flexed, with the patient's eyes shut, and he was asked to give the position of his right forearm, he stated that it was "straight out" and was greatly surprised at his wrong answer when allowed to open his eyes. There was definite loss of passive position at the hip, knee- and ankle-joints, and the patient was unable to appreciate the position of his legs when movements of these joints were made. The great toe joints, however, appeared to have preserved the sense of passive position, as in a large number of trials on both sides he was uniformly right in his answers as to the position of the great toe.

Appreciation of weight: This was tested by placing weights in the palms and allowing the patient to move the hand up and down.

He could tell that 1 lb. was heavier than $\frac{1}{2}$ lb., but was unable to distinguish between 1 lb. and $\frac{1}{2}$ lb.

Localization by naming the spot stimulated seemed to be good, but if the patient was asked to place his finger on a point touched on his opposite arm he generally hit a point one to two inches away from the place stimulated. It should, however, be remembered that this method of testing localization of points touched on the skin necessitates a perfect sense of passive position and movement and in this patient's arms this was gravely defective.

On the palms the patient was entirely unable to distinguish whether he was touched by one point or two points of a pair of compasses.

The skull and spinal column were normal, and there was control of the sphincters until the last few days of his life.

He was treated by arsenic internally. On December 2 he was given 5 minims of Fowler's solution three times a day, and on December 9 this was increased to 8 minims three times a day.

The teeth were treated with antiseptic lotions and potassium chlorate paste. A streptococcus was isolated from the mouth, and a vaccine prepared. On December 13 twenty-five million were injected, on December 17 a further twenty-five million, and the dose was again repeated on December 23. There was no febrile or other reaction to this treatment.

The course of the patient was steadily downhill. On admission he weighed 7 st. 6 lb.; on December 7, 7 st. 5 lb. 5 oz.; on December 14, 7 st. 2 lb. 8 oz., and on December 21, 6 st. 7 lb.

Towards the end he complained of a good deal of generalized abdominal pain, and he developed bronchitis. Later he became noisy at night and had several severe heart attacks, in one of which he died on December 27.

POST-MORTEM EXAMINATION.

The summary of the findings at the necropsy, made on the following day, is as follows:—

Post-mortem, December 28, 1910.

Hypostatic bronchopneumonia. Subacute combined degeneration of spinal cord. Severe anæmia. Granulomatous ulcer of stomach.

Chronic bronchitis and emphysema. Acute mucopurulent bronchitis, slight peribronchial pneumonia and gross œdema in both lower lobes of lungs; most definite in right lower lobe. Fibrous pleural adhesions over right lung. Large ulceration in pyloric region of stomach. Infiltration

of glands of greater and lesser curves. *Hyperplasia of red marrow in femur. Red marrow throughout vertebrae and sternum. Edema and parenchymatous degeneration of liver (1.533 kgm.). Macroscopic reaction for free iron negative, in both liver and spleen (106 grm.). Parenchymatous degeneration of kidneys (419 grm.). Simple atrophy of heart (255 grm.). Fatty "tigerling" of papillary muscles of left ventricle. A few streaks of fatty atheroma in aorta; calcareous atheromatous plaque in anterior descending coronary. Inspissated pus in tonsils. Peri-appendicular fibrous adhesions. Great marasmus.*

The stomach contained some yellowish fluid. The mucosa was ulcerated over a large area, which almost encircled the organ and reached to within $1\frac{1}{2}$ in. (3.8 cm.) of the pyloric sphincter. The edges of the ulcer were everted and felt hard. The base of the ulcer was thin, being formed to a large extent by subserosa; it was covered by a greyish-yellow necrotic tissue. On the serous surface, corresponding to the ulcer, were fibrous adhesions. The glands upon the greater curvature were enlarged to the size of sparrows' eggs and felt hard. Their cut surface was firm, granular and white. The glands on the lesser curve were rather smaller than wrens' eggs. Their cut surface was granular and of a greyish-yellow colour.

Microscopical Examination of the Stomach.—Sections were made from two portions of the edge of the ulcer. At the border of the ulcer the submucosa is thickened and the ulceration extends for a little way into it, undermining the mucosa. The base is formed near the border by muscularis and towards the centre by subserosa. The whole of the ulcerated surface shows a broad zone of necrosis, in which lie very large numbers of long, unbranched, Gram-positive mycelial threads. These pass vertically from the surface into the necrotic tissue. Amongst them are some Gram-positive cocci, diplococci, and bacilli. Below this there is a cellular zone. At the border this consists of plasma-cells, lymphocytes, eosinophile leucocytes, and mast-cells in a network of spindle fibroblasts and delicate collagenous fibrils. In the base, especially towards the centre, the delicate collagenous fibrils enclose groups of large free cells. The surface area of these cells is on an average equal to one and a half to two and a half red corpuscles. They are usually round or slightly angular, but short spindle forms are also present. The nucleus occupies three-quarters or more of the cell. It is round or oval, and occasionally indented, so as to have, on focusing, a lobed appearance. The membrane and chromatin fibrils are delicate and deeply stained, the latter forming a finely meshed net. Most of the cells have two or three conspicuous nucleoli. In some cells there are two hemispherical nuclei set close together. Rarely there are several superimposed nuclei. There are considerable numbers of karyokineses. In the wall of the stomach beneath this zone there are numerous large spindle fibroblasts and a great infiltration by plasma-cells, lymphocytes, eosinophile leucocytes, and mast-cells. This infiltration extends through to the serous surface, occupying the interstitial septa of the muscularis.

At first sight the cellular zone in the base of the ulcer suggested the remnant of an ulcerated medullary carcinoma. In structure, however, the cells are unlike epithelial cells, and were readily distinguished from those of medullary carcinomata with which they were compared. They closely resemble the subjacent fibroblasts and merge into these. They are nowhere arranged as a lining to tubules, nor is there a true alveolar formation. Moreover, they lie in a zone which is confined to the base of the ulcer. They do not form nodules in the muscularis or serosa beneath this zone. They do not infiltrate the submucosa at the border of the ulcer. They are not found within lymphatics.

The *meninges and brain* showed no abnormality. In sections of the fresh cord no areas of degeneration could be recognized. Since fixation in formalin, however, pearly-white areas of degeneration are visible, which contrast sharply with the grey matter and the rest of the white matter. The grey matter has a yellowish tint, while the rest of the white matter is of a still deeper yellow colour. In the upper lumbar cord a small rounded pearly-white area lies in the centre of each posterior column. In the thoracic region the pearly areas are fused to form a single area of much larger dimensions. The pearly-white degeneration in the posterior columns is visible as far as the gracile and cuneate nuclei. Below the seventh thoracic segment, and in most sections above the fourth thoracic segment, a narrow zone of unaltered white matter can be recognized between the areas of degeneration and the posterior horns. In the sixth thoracic segment a pin-point, pale dot is just visible to the naked eye in the position of the lateral pyramidal tract on the right side. This dot is not of so pure a white colour as the area in the posterior column. In no other segment can an abnormal area be recognized in the lateral or anterior columns.

MICROSCOPICAL EXAMINATION OF CORD, MEDULLA AND MESENCEPHALON.

Immediately after removal the mesencephalon, medulla and cord were incised and placed in 5 per cent. formalin. After fixation for a few days a series of portions was removed from the cord. The portions were treated in the following manner: (1) Hardened in Müller's fluid for three months, stained in Busch's modification of Marchi's solution and embedded in celloidin. (2) Hardened in Müller's solution, embedded in paraffin and stained by Mann's modification of the Weigert-Pal method, by Ehrlich's hæmatoxylin and eosin, and by Weigert's iron hæmatoxylin and van Gieson.

Seven months after death a second series of portions from the cord was embedded in paraffin and stained with hæmatoxylin and eosin, and by the methods of Weigert-van Gieson, Weigert-Gram, Twort and Lenhossek.

Eight months after death a third series was removed from the cord, medulla

and mesencephalon. These portions were: (1) Fixed for six days in Müller's fluid, stained in Busch's modified Marchi's solution and embedded in celloidin; (2) mordanted in Weigert's fluorchrome mixture, embedded in paraffin and stained by Mann's modification of the Weigert-Pal method.

Third sacral segment (Weigert-Pal and Marchi, third series).

Weigert-Pal.—The medulla of a few fibres is seen to be swollen when examined under high powers.

Marchi.—A few scattered fibres show fatty degeneration. These fibres are seen especially in the posterior columns, the lateral pyramidal tracts and the ventral pyramidal tracts. A very few fibres in the anterior and posterior roots show degeneration.

Fifth lumbar segment (Marchi, third series). The appearances are very similar, save that fibres showing degeneration by the Marchi method are more numerous in the posterior columns.

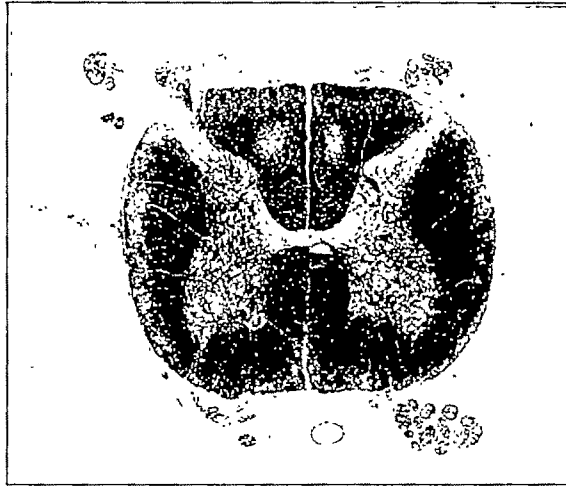


FIG. 1.—Section through the third lumbar segment stained by the Weigert-Pal method. The section shows two small rounded areas of vacuolar degeneration in the centre of the posterior columns.

The second and third lumbar segments (Weigert-Pal and Marchi, first series; fig. 1).

Weigert-Pal.—The centre of each posterior column contains a small rounded area in which the neuroglia forms a wide-meshed net enclosing large, vacuolar spaces. In a few of these spaces there are fibres with a swollen medullary sheath which is not stained at all, or is stained faintly by hæmatoxylin. In others there are fragments of a substance which is stained faintly by hæmatoxylin.

In the rest of the white matter only a few fibres with swollen or disintegrated medulla can be found under the higher powers.

Marchi.—There is very little evidence of additional degeneration. There are a very few degenerated fibres scattered through the white matter. They are most numerous in the posterior columns and the lateral and ventral pyramidal tracts. The greatest number are present in the lateral pyramidal tracts. In the posterior columns the majority lie close to the dorsal septum. The medullary sheath of one or two fibres in the zone of entry of the posterior roots is stained.

The anterior and posterior roots show no degeneration.

Ninth thoracic segment (Weigert-Pal and Marchi, first series; fig. 2).

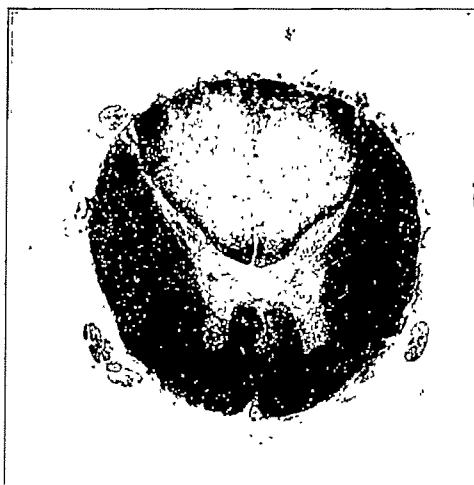


FIG. 2.—Section through the ninth thoracic segment stained by the Weigert-Pal method. The section shows much degeneration of the greater part of the posterior columns. There are a few scattered vacuolar spaces in each lateral column.

Weigert-Pal.—There is a large heart-shaped area of degeneration in the posterior columns. This is separated from the posterior grey commissure and the dorsal horns by a narrow zone of unaltered fibres. A broader zone of unaltered fibres separates it from the dorsal surface of the cord. There is also a narrow zone on each side of the dorsal septum in which there are considerable numbers of fibres which are not degenerated. The heart-shaped area appears, therefore, to be formed by two discrete areas of degeneration which have almost fused in the mid-line. The degenerated area is vacuolar, but the majority of the vacuoles are smaller than those seen in the lumbar segments. Vacuolation is most conspicuous in the periphery of the degenerated area. The vacuoles frequently contain portions of a substance which is stained very faintly but gives the same staining reaction as myelin. Transitions can be seen between spaces containing this substance and single nerves, or groups of nerves, with greatly swollen, faintly stained, medullary sheath.

In both lateral columns in the region of the pyramidal tracts there are

a few scattered, clear, vacuolar spaces. Some of these contain fragments of myelin. In the rest of the lateral and in the anterior columns there are only a very few fibres with swollen or disintegrated medulla.

Marchi.—There are many large cells loaded with granules of fat in the more central part of the degenerated area in each posterior column. These fat-granule-cells also occasionally contain fragments of myelin. In the periphery of each degenerated area there are considerable numbers of extracellular droplets of fat and of medullary sheaths which are stained by osmic acid. This recent degeneration is especially evident in the narrow zone on either side of the dorsal septum. A little fatty degeneration is also present in the posterior columns in the zone of fibres which did not show degeneration in the Weigert-Pal sections. The dorsal portion of the zone is most affected.

There is a very little fatty degeneration in and around the vacuoles in the lateral and pyramidal tracts. In the rest of the white matter there are a few degenerated fibres. These are most numerous in the ventral pyramidal tracts.

There is no degeneration in the anterior and posterior roots.

Between sixth and seventh thoracic segments (hæmatoxylin, eosin and van Gieson).

In this section there are no fibres entering from the posterior roots. The area of vacuolar degeneration in the posterior columns is considerably larger. It touches on both sides the fibrous trabecula which passes from the dorso-lateral sulcus to the posterior horn. It also extends nearer the dorsal surface, reaching the surface at one spot in the right posterior column.

There are a few scattered vacuolar spaces in both lateral pyramidal tracts. They are more numerous on the right side.

Sixth thoracic segment (Weigert-Pal and Marchi, third series).

Weigert-Pal.—Posterior roots are not included in the section. The area of degeneration in the posterior columns is slightly less extensive than in the preceding section. It reaches only on the right side the fibrous trabecula which extends from the dorso-lateral sulcus to the posterior horn. It almost reaches the outer surface of the cord in the centre of each posterior column. Vacuolation is most conspicuous in the periphery.

In the right lateral pyramidal tract there is much more vacuolar degeneration than in the preceding section. In the centre of the tract there is a rounded group of vacuoles, and scattered round this there are isolated vacuoles. The degeneration in some sections appears to affect more than a third of the tract. In the left lateral pyramidal tract there are very few vacuoles.

Marchi.—Posterior roots are present. The area of vacuolar degeneration is separated everywhere from the posterior horns, the posterior grey commissure and the dorsal surface of the cord by a zone of fibres. The area of vacuolar degeneration contains large numbers of fat-granule-cells. The vacuolation is most marked in the periphery of the area. In the zone of fibres surrounding this area there is considerable fatty degeneration. The greatest number of degenerated fibres is present in the dorso-mesial and ventro-mesial portions of the zone.

In the right lateral pyramidal tract the area of vacuolation is not so large as in the Weigert-Pal sections. It contains a group of fat-granule-cells. In the left lateral pyramidal tract one or two vacuoles are present in some of the sections. There are many fibres showing fatty degeneration in the right lateral pyramidal tract and a considerable number in the left.

Fibres showing fatty degeneration are scattered through the rest of the periphery of the cord. They are most numerous in the ventral pyramidal and Gowers's tracts.

A very few degenerated fibres are present in the intramedullary portion of the posterior roots. One or two degenerated fibres are present in the extramedullary portion of the roots.

Third thoracic segment (hæmatoxylin, eosin and van Gieson).

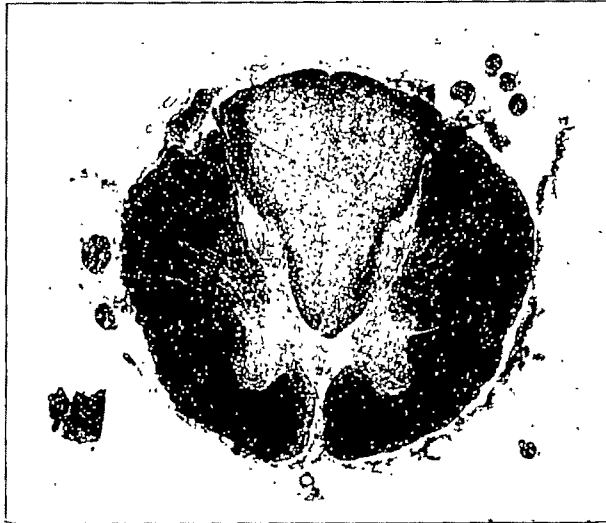


FIG. 3.—Section through the second thoracic segment stained by the Weigert-Pal method. The section shows degeneration of the central parts of the posterior columns, and slight degeneration in the lateral pyramidal tracts.

A few fibres enter from the posterior roots. The area of vacuolar degeneration in the posterior columns is of very similar extent. It extends on each side to, but does not involve, the bundle of fibres entering from the posterior roots.

In the left lateral pyramidal tract there is a small group of vacuoles and a few scattered vacuoles can be seen in the right.

Second thoracic segment (Weigert-Pal and Marchi, first series; fig. 3).

Weigert-Pal.—The area of degeneration in the posterior columns is considerably smaller and is separated everywhere from the entering fibres of the posterior roots and from the dorsal horns by a zone of unaltered fibres.

In the lateral pyramidal tracts the degeneration resembles that of the

previous segment. The vacuoles form a small group on the left side. There are a few scattered vacuoles on the right side. The smallest vacuoles contain an axis-cylinder with a swollen medulla. Some of the larger contain fragments of myelin. In the rest of the white matter there are a very few fibres with swollen medulla.

Marchi.—Cells loaded with granules of fat are scattered throughout the degenerated area in the posterior column. Some extracellular droplets of fat and medullary sheaths stained by osmic acid are also present. These are especially numerous in the periphery. A considerable amount of fatty degeneration is present in the posterior columns in the zone of fibres which

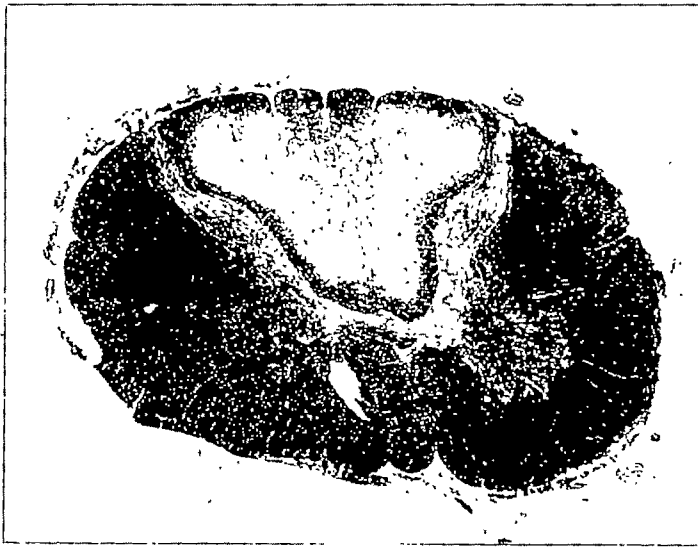


FIG. 4.—Section through the fifth cervical segment stained by the Weigert-Pal method. Much degeneration of the central parts of the posterior columns. Burdach's column more affected than the column of Goll.

appeared unaltered in the Weigert-Pal stain. Some recent degeneration is also seen in the ventral pyramidal tracts and the periphery of the lateral columns, including Lissauer's zone. There is very little recent degeneration in the lateral pyramidal tracts.

There is no degeneration in the anterior and posterior roots.

Fifth cervical segment (Weigert-Pal and Marchi, first series; fig 4).

Weigert-Pal.—The degenerated area in the posterior columns is separated from the posterior grey commissure and horns by a zone of unaltered fibres. It touches the zone of entry of the posterior roots on the left side. The column of Burdach is more degenerated than the column of Goll. Vacuolation is very marked in Burdach's column and is much more conspicuous than in the column of Goll. In the ventral two-thirds of the degenerated area, at the

junction of the columns of Goll and Burdach, there is an area on each side in which there is very little vacuolation, but in which the degeneration of the fibres is extreme.

In the lateral columns, in the position of the lateral pyramidal tracts, there is much less degeneration than in the preceding segment. There is an ill-defined group of eight or ten vacuoles on the left side and still fewer on the right.

In the remainder of the white matter there are a very few scattered fibres which show swelling and occasionally disintegration of the medullary sheaths.

Marchi.—Fat-granule-cells are present in the degenerated area in the posterior columns. These cells are very numerous in the portion which shows

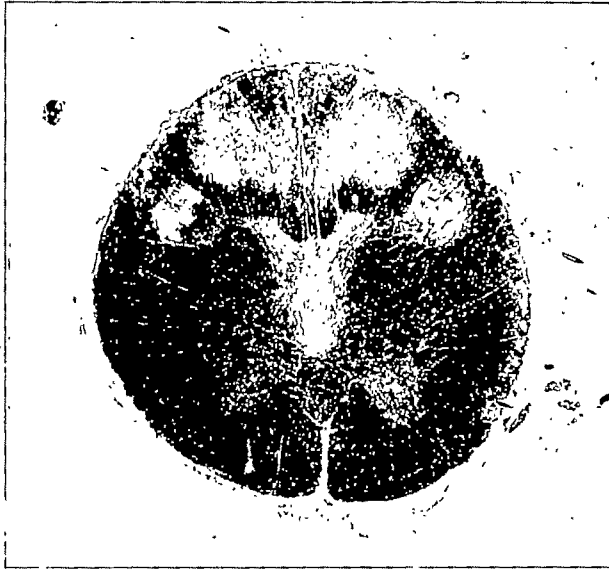


FIG. 5.—Section through the first cervical segment stained by the Weigert-Pal method. The section shows great degeneration of Burdach's column. The column of Goll is less affected, and the rest of the cord is normal, save for a very few degenerated fibres, which can only be discovered with high power.

very little vacuolation. There is very little fatty degeneration in the surrounding zone of fibres which appeared unaltered in Weigert-Pal. The dorsal and ventromesial portions of the zone are most affected. There are a few droplets of fat in the zone of entry of the posterior roots.

There is no evidence of fatty degeneration in the lateral pyramidal tracts. A little fatty degeneration is present, however, in all the tracts in the periphery of the lateral and anterior columns, especially in Gowers's tract.

A few droplets of fat are present in the intramedullary fibres of the anterior roots and in the extramedullary fibres of the posterior roots. Very few are present in the extramedullary fibres of the anterior roots.

First cervical segment (Weigert-Pal and Marchi, first series; fig. 5).

Weigert-Pal.—The decussation of the pyramidal fibres is present. The degenerated area in the posterior columns is separated from the posterior grey commissure and horns by a layer of unaltered fibres. The column of Burdach is much more degenerated than the column of Goll. The dorsal half of the latter is little affected. Vacuolation is much more prominent in Burdach's column than in Goll's and is very evident in the periphery of the degenerated area in Burdach's column.

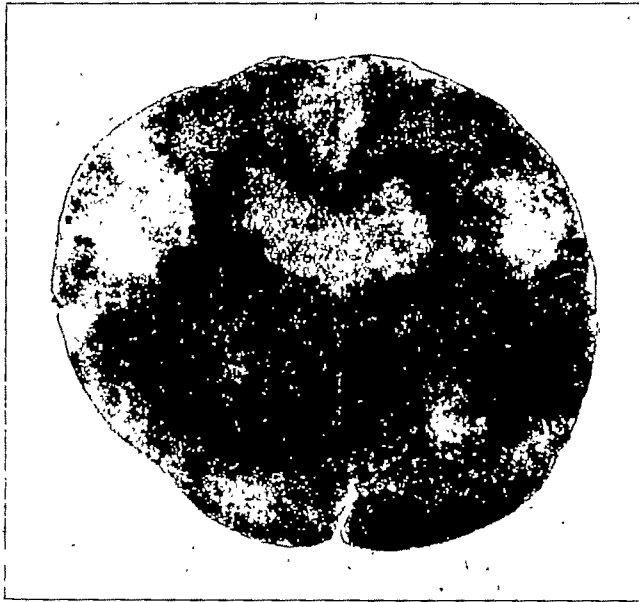


FIG. 6.—Section of medulla, 1.2 cm. below olivary eminences. Stained by Marchi's method. Conspicuous comma-shaped area of degeneration in each funiculus cuneatus. The restiform body is almost unaffected, and in the remainder of the white matter only a very few scattered fibres are degenerated.

In the left lateral column, in the position of the lateral pyramidal tract, there is a small group of small vacuolar spaces. One or two vacuolar spaces are seen in some sections in a similar position on the right side. In the remainder of the lateral and anterior columns there are a very few scattered fibres in which the medulla is swollen and pale, and occasionally disintegrated.

Marchi.—In the centre of the degenerated area in Burdach's column and throughout the affected portion of Goll's column there are large numbers of fat-granule-cells. Where the vacuolation is marked, fat-granule-cells are rare. A few extracellular droplets of fat are present in the periphery of the area of degeneration. In the portion of the posterior columns which appeared unaltered with Weigert-Pal's stain there is considerable degeneration in the

form of fat-droplets or fatty medullary sheaths. This is most distinct in the dorsomesial and ventromesial portions of the posterior columns. A very little degeneration is present in the zone of entry of the posterior roots.

There is a little scattered, fatty degeneration in the lateral pyramidal tracts and in the rest of the lateral and anterior columns, especially in the periphery. The greatest number of the degenerated fibres lie in the dorsal spino-cerebellar tracts and the mesial aspect of the anteromesial columns.

There is no degeneration in the anterior and posterior roots.

Medulla, 1.2 cm. below olivary eminences (Marchi, third series; fig. 6).

This segment includes the pyramidal decussation near its centre. The funiculus gracilis is triangular in shape. The gracile nucleus occupies about two-thirds of its surface. The funiculus cuneatus is quadrilateral with concave ventromesial boundary. A small portion of the cuneate nucleus is present within it on the left side, occupying a ventrolateral position.

In the centre of the funiculus cuneatus on each side there is a conspicuous area of degeneration. This area is semilunar in shape with its concavity ventromesial. Its dorsal extremity encroaches in the lower sections upon the most external portion of the ventral extremity of the funiculus gracilis. It contains very large numbers of fat-granule-cells. Vacuoles are present, especially in the periphery. Where the vacuoles are abundant the fat-granule-cells are scarce.

In the remainder of the funiculus cuneatus scattered fibres show fatty degeneration. A considerable number of degenerated fibres are present in the funiculus gracilis. Some degenerated fibres are also found in the rest of the white matter.

Medulla, 1 cm. below the olivary eminences (Marchi, third series).

This segment includes the upper part of the pyramidal decussation. The gracile nucleus is larger and occupies the greater part of the funiculus gracilis. The fibres of the funiculus cuneatus form a narrow oblong mass with processes extending ventromesially on either side of a large cuneate nucleus.

Within the funiculus cuneatus there is a conspicuous semilunar area of degeneration. This embraces the external border of the cuneate nucleus, but is separated from the nucleus by a zone of fibres of which few show degeneration. This zone becomes narrower in sections nearer the cerebrum. The degenerated area contains large numbers of fat-granule-cells. It has a somewhat spongy appearance, owing to the presence of vacuoles. The vacuoles are, however, relatively small and inconspicuous.

In the remainder of the funiculus cuneatus and in the funiculus gracilis a considerable number of fibres show fatty degeneration. A few scattered degenerated fibres are also present in the lateral and anterior white matter.

Medulla, 8 mm. below the olivary eminences (Weigert-Pal, third series).

The central canal is still closed. The accessory cuneate nucleus, a small portion of the inferior olivary nucleus, and the inner accessory olivary nucleus are present.

In the funiculus cuneatus there is a pale area of degeneration. It is semi-

lunar in shape and lies upon the dorsal and lateral surfaces of the cuneate nucleus, terminating on the mesial aspect of the dorsal half of the accessory cuneate nucleus. The area contains small vacuolar spaces, and fibres with pale, swollen medulla.

Medulla, 6 mm. below the olivary eminences (Marchi, third series).

The central canal has opened out. The inferior olivary nucleus shows its characteristic form. The nuclei of the eleventh and twelfth cranial nerves are present.

Immediately external to the cuneate nucleus is a narrow semilunar area occupied by fat-granule-cells. From this a narrow band of fat-granule-cells passes along the external surface of the accessory cuneate nucleus.

A few fibres in the rest of the white matter show fatty degeneration. The majority are present in the pyramidal tracts.

Medulla at inferior extremity of olivary eminences (Weigert-Pal, third series).

The cuneate nucleus is still present. There is no visible degeneration in the sections.

Medulla, through centre of olivary eminences (Weigert-Pal and Marchi, third series). There is no visible degeneration by the Weigert-Pal method, but by Marchi's method a few fibres in the pyramids show fatty degeneration.

At and above centre of pons (Weigert-Pal and Marchi, third series).

Weigert-Pal.—There is no visible degeneration.

Marchi.—The sections are not completely permeated by the stain. They are taken below the level of the Weigert-Pal sections, and the lowermost touch the cephalic extremity of the superficial origin of the fifth cranial nerve on the right side. Some intramedullary bundles of fibres of the fifth nerve are present on the right side. A large number of these fibres are swollen and stained by the osmic acid.

Mid-brain, through upper extremity of peduncles, red nucleus, anterior corpora quadrigemina, and posterior extremity of the optic thalamus (Weigert-Pal and Marchi, third series).

Weigert-Pal.—The intra- and extra-medullary fibres of the third nerve show moniliform swellings of the medullary sheath. The swellings are frequently not stained.

Marchi.—The swellings in the medullary sheaths of the third nerve are stained by osmic acid. There is no degeneration in the peduncles.

Neuroglia, vessels, and nerve-cells.

The network of glia-fibres is rarefied in the areas of vacuolar degeneration. The fibres are swollen and ragged. There is no evidence of proliferation of the fibres. The glia-cells appear to be reduced in number, but increased in size.

The artery of the posterior septum shows hyaline degeneration of the media within the degenerate areas. There is no thrombosis, endarteritis, or hæmorrhage. The posterior septum is infiltrated in places by a few cells of lymphocytic type or by numerous fat-granule-cells.

The nerve-cells of the anterior, lateral, and posterior horns, and of Clarke's

column, are of good shape and contain a centrally placed nucleus. Almost all the cells contain granules of pigment. The pigment is arranged in the form of clumps upon one or two sides of the nucleus, or completely encircles the nucleus. This pigment is present also in the cells of the medulla. In sections taken from the lumbar, upper and lower thoracic and cervical cord, and stained by Lenhossek's method, the remainder of the protoplasm and the dendrons are occupied by Nissl's granules. These are, almost invariably, arranged evenly and of good shape. In a few cells they are pyknotic. In one or two large cells in the lumbar cord, in the position of Stilling's nucleus, the nucleus is eccentric, and there is central chromatolysis.

No *organisms* were detected in sections stained by the methods of Twort and Weigert-Gram.

SUMMARY OF MICROSCOPICAL CHANGES.

Two expressions of degeneration may be distinguished in the sections of the central nervous system: (1) A vacuolar degeneration which is visible in sections stained by the methods of Weigert-Pal and Marchi; (2) a fatty degeneration which is only recognized in sections stained by the method of Marchi.

(1) The vacuolar degeneration is confined to the posterior columns of the cord and medulla and to the lateral columns of the cord. In the posterior columns this degeneration stretches from the third lumbar segment to a short distance behind the cephalic extremity of the cuneate nucleus. In the lumbar cord it occupies a small area in the centre of each posterior column. At the level of the ninth thoracic segment these two areas become fused in the middle line. They now occupy the whole of both posterior columns with the exception of a circular zone of fibres which lies beneath the dorsal surface of the cord and covers the mesial and dorsal surfaces of the posterior horns and posterior grey commissure. From the junction of the sixth and seventh thoracic segments to the third thoracic segment the area is larger. It extends to the bundle of fibres entering from the posterior roots but does not involve it. Where this bundle is absent, it extends to the fibrous trabecula which passes from the dorsolateral sulcus to the posterior horn. Moreover, it extends nearer the dorsal surface of the cord. At the level of the second thoracic segment the area contracts again considerably. It is separated from the entering fibres of the posterior roots by a well-defined zone of fibres. In the fifth cervical segment it has a similar extent, but the degeneration in the column of Goll is much less intense. In the first cervical segment the column of Goll is even less affected. In the medulla the external portion of the ventral

extremity of the funiculus gracilis is affected in a few of the lowermost sections. Above this the funiculus gracilis is free. Within the funiculus cuneatus the area of degeneration is continued almost to the cephalic extremity of the cuneate nucleus.

A similar vacuolar degeneration is found in the lateral pyramidal tracts from the ninth thoracic segment to the first cervical segment. In the sixth thoracic segment alone is the area of considerable size and just visible to the naked eye. Here on the right side in one of the sections removed from this level the area appears to occupy rather more than a third of the tract. From the ninth to the sixth thoracic segment and from the sixth to the first cervical segment the degeneration is represented by a few vacuoles only. They are in general more numerous on the left than the right side. They are usually scattered and may be absent in some of the sections cut from a single block. They are aggregated into small groups in the third and second thoracic and first cervical segments on the left side.

In the rest of the white matter there is no definite vacuolar degeneration. A few fibres, however, in Weigert-Pal sections show a swollen, or even disintegrated medullary sheath. These fibres probably represent an early stage of vacuolar degeneration.

Macroscopical and microscopical examination shows that the area of vacuolar degeneration in the posterior columns of the cord and medulla forms a continuous column, which is of greatest diameter between the ninth and second segments of the thoracic cord. In the lateral columns, however, the degeneration is focal, varying in extent in different sections and being absent from some sections.

In the areas of vacuolar degeneration the following sequence of changes can be deduced from examination of sections stained by Weigert-Pal or Weigert's iron-haematoxylin. The medullary sheath of one or more fibres becomes more and more swollen and loses its affinity for haematoxylin. Finally, the medullary sheath or sheaths disappear, leaving a vacuolar space, in which there may be some fragments of faintly stained myelin. The axis-cylinder, as a rule, undergoes less rapid degeneration than the medullary sheath. It ultimately disappears. The network of glia-fibres becomes rarefied by the formation of the vacuoles. The most conspicuous vacuoles are present in the lateral pyramidal tracts and in the periphery of the degenerated area in the posterior columns. In the more central portions of the degeneration in the posterior columns the vacuoles are, as a rule, smaller, and the network of glia is of narrower mesh. There is no evidence, however, of proliferation of glia-fibres or cells.

(2) In Marchi preparations the areas of vacuolar degeneration contain fat-granule-cells, extracellular droplets of fat and fatty medullary sheaths. The granule-cells also occasionally contain fragments of myelin. The fat-granule-cells are very numerous throughout the more central portions of the area of degeneration in the posterior columns of the cord and medulla. They are less numerous in the periphery. Extracellular droplets of fat and fatty medullary sheaths are relatively few. They are confined chiefly to the periphery of the area. In the lateral pyramidal tracts extracellular droplets of fat and fatty medullary sheaths are present in small numbers. Fat-granule-cells are only found in the centre of the large area of degeneration, in the sixth thoracic segment on the right side. From examination of the Marchi sections it appears that numbers of the vacuoles are formed by a swelling and disintegration of the medullary sheath without a fatty metamorphosis.

A fatty degeneration is also demonstrated by the Marchi method in the white matter where it is not affected by the vacuolar degeneration. In general there is very little of this degeneration. It is expressed usually by a blackening and slight swelling of the medullary sheath. Free droplets of fat are much less common.

In the zone of fibres in the posterior columns which surrounds the area of vacuolation this fatty degeneration is relatively abundant. It is most extensive where the zone meets the vacuolar degeneration; in the more peripheral part of the zone degenerated fibres are scarce. The degeneration is greatest in the dorsomesial and ventromesial portions of the zone. The degeneration is also present in a corresponding position in the medulla, in the funiculus cuneatus and funiculus gracilis. Both in the cord and medulla the degeneration extends beyond the segments in which vacuolar degeneration is present. Thus several degenerated fibres are found in the posterior columns in the fifth lumbar segment, and a few in the third sacral. A few are present throughout the funiculus gracilis.

In the lateral pyramidal tracts degenerated fibres are found in the neighbourhood of the vacuolar degeneration. They are less numerous than in the corresponding position in the posterior columns. The greatest number is present in the sixth thoracic segment on the right side. Scattered degenerated fibres are also present in the lateral pyramidal tracts in segments in which the vacuolar degeneration is absent; that is, in the third sacral and fifth lumbar segments. They can also be recognized in the pyramidal tract above the decussation as far as the centre of the olivary bodies.

A few scattered, degenerated fibres are also present in the remainder of the lateral and anterior columns of the cord and medulla. They are almost confined to the periphery. Their number and the position in which the majority are present vary in different segments. In general they are most numerous in the position of the ventral pyramidal tracts. In the anterolateral region they are usually few in number. They are more numerous in Gowers's tract than in the dorsal spinocerebellar tract.

In some sections there is a very little degeneration of the fibres of the posterior roots as they pass forwards on the mesial surface of the dorsal horns. A still slighter degree of degeneration is found in the extra-medullary portions of the posterior roots in some segments. In the second and third lumbar, the ninth thoracic, the second thoracic and the first cervical segments there is no trace of degeneration in the extra-medullary portions of the posterior roots.

A few degenerated fibres are present in the anterior roots in the third sacral, fifth lumbar, and fifth cervical segments.

No significance can be attached to the degeneration of the fibres of the fifth and third cranial nerves; for such changes are known to occur repeatedly in these nerves when there is no reason to suppose that they were diseased during life.

The nerve-cells in the cord, medulla and mesencephalon contain much granular pigment. Evidence of other degeneration is very exceptional. In a few cells the granules of Nissl are pyknotic. In one or two large cells in the lumbar cord, in the position of Stilling's nucleus, the nucleus is eccentric and there is central chromatolysis.

There is no evidence that the degeneration was due to changes in the vessels. Bacteria were not detected.

THE NATURE OF THE PATHOLOGICAL CHANGES.

The condition affecting the spinal cord and medulla is evidently a degeneration similar to that which has been called by Russell, Batten and Collier [8] "subacute combined degeneration."

The case is exceptional in the almost complete limitation of the degenerative process to the posterior columns. There is, however, slight degeneration within the lateral columns in the areas occupied by the lateral pyramidal tract, so that the term "combined degeneration" is justified.

The presence of fat-granule-cells in large numbers within the areas of degeneration is evidence of the acute nature of the process in this case. Death has occurred in a comparatively early stage of the disease.

This accords with the observation of Farquhar Buzzard [1] that "the prognosis with regard to the duration of life is somewhat better in those patients who present predominating lateral column signs, than in those in whom the posterior columns appear to be more severely affected."

As in almost all reported cases, the changes in the central nervous system were associated with a severe anæmia. In this case the anæmia apparently preceded the affection of the cord. The duration of the illness was three months. The first symptom noticed was anæmia, and this was followed a fortnight later by the onset of nervous troubles. The anæmia was of a severe secondary type. As in most of the other reported cases, the colour index was high, 1.1 on December 2, and 1.4 on December 23. Degenerated red cells were numerous. There were large numbers of normoblasts, but megaloblasts were absent. *Post-mortem* there was an excess of red marrow in the femur, but it was not present in the quantity characteristic of a typical case of pernicious anæmia. Further, the reaction for free iron in the liver was absent. According to Collier [3] this reaction has never been found in a case of subacute combined degeneration.

With the exception of hyaline degeneration of the media of the artery of the dorsal septum, within the degenerated area, there was no evidence of vascular lesions in the spinal cord. There were no hæmorrhages. The changes in the cord differ fundamentally from those which are known to be secondary to severe anæmia. There is no evidence of inflammation. The case supports the view expressed by Collier [3] and others, that in subacute combined degeneration the anæmia and spinal degeneration are related, not as cause and effect, but as concomitant effects of a single pathological process, and that this pathological process is toxic in nature. As regards the source of the toxin a very large, infected, granulomatous ulcer was found in the stomach at the necropsy. The ulcer gave no symptoms during life, so that it is impossible to estimate its duration from clinical data. The fibrous adhesions, however, on the base of the ulcer, and the histological characters of the ulcer, show that it was chronic in nature. These characters suggest that the ulceration preceded the onset of the anæmia and nervous symptoms. It is therefore probable that the toxic agent was absorbed from this ulcer.

In other cases lesions have been found in the alimentary canal. Collier [3] states: "Septic gingivitis and stomatitis are common, signs of chronic gastro-enteritis are occasionally present, and more rarely there are ulcers in the large intestine."

Too great importance should not, however, be attached to the state of the mouth and gums. Sepsis of the mouth and gums is frequently secondary to anæmia. Further, among the lower classes a filthy condition of the mouth is unfortunately only too common, and the possessors usually live for years without any evidence of secondary lesions. In the present case vaccines prepared from the septic mouth had no effect upon the course of the disease. It is, therefore, to the ulcer of the stomach, rather than to the septic gums, that the probable entry of the toxic agent should be ascribed in the present case.

THE RELATION OF THE ANATOMICAL CHANGES IN THE SPINAL CORD AND MEDULLA TO THE SYMPTOMS OBSERVED DURING LIFE.

The chief lesion in the spinal cord was a profound degeneration of the central parts of the posterior columns. The posterior root zone had escaped save for a little recent degeneration of the medulla of a few fibres. The destruction had been limited to the long fibres of the posterior columns. With the possible exception of the third to sixth thoracic segments, it left intact those fibres of the posterior columns which run upwards for a short distance preparatory to entering the grey matter of the posterior horn. Moreover, the other afferent tracts in the spinal cord were almost unaffected. Only a very few scattered fibres showed degeneration by Marchi's method in the ventral spinocerebellar, the spinothalamic and the dorsal spinocerebellar tracts. The case therefore presents a unique opportunity for studying the effects of a lesion of the long fibres of the posterior columns.

The main loss was in the appreciation of passive position, which was almost entirely absent in both upper limbs and gravely defective for movements of the hip, knee and ankle. It is, however, noteworthy that the patient was always able to state correctly the position of both great toes. This may be due to the fact that in the lumbar region the lesion was much less advanced than in the cervico-thoracic part of the spinal cord, and that even in the thoracic part of the cord the dorsal portion of the column of Goll was almost intact; this probably allowed sensory impulses from the sacral roots and great toe to ascend the spinal cord without difficulty.

This case, therefore, demonstrates that a lesion of the posterior columns alone, without any affection of the other spinal afferent tracts, produces profound loss of the sense of passive position. This conclusion is in exact agreement with that arrived at by Head and Thompson [4].

Pétren [7], however, has lately brought forward the view that there is a double path in the spinal cord for the sense of passive position; according to him these impulses may pass up either in the posterior column of the same side or in the dorso-cerebellar tract (K.S.B.) of the same side. He says, "Die ganze Erfahrung bei den Fällen von Stichverletzung wird also gut erklärt, wenn wir zwei Bahnen für den Muskelsinn annehmen und zwar beide gleichseitig, die eine im Hinterstrange und als die andere die K.S.B., und ferner annehmen, dass sie einander so gut ersetzen, dass der Wegfall der einen keine auffallende Störung des Muskelsinnes zur Folge hat."

Most of Pétren's cases, however, have been collected from the literature, and in many of them the distinction between ataxia and loss of the sense of passive position has not been clearly made. It is, of course, possible to have ataxia without any loss of the sense of passive position, although a loss of the latter form of sensibility is always accompanied by more or less ataxia.

In the present case the cerebellar tracts were only affected by a very slight and recent degeneration, and therefore the findings in this case are strongly opposed to Pétren's view, and in favour of that of Head and Thompson, and most English observers, that the impulses underlying the sense of passive position pass up in the posterior columns, while the impulses passing up in the cerebellar tracts are non-sensory afferent impulses concerned in the maintenance of equilibrium and muscular tone.

The loss of tactile discrimination (compass test) and the impairment of the power of appreciating weights are also interesting, and are in this case associated with a lesion of the long fibres of the posterior columns.

Localization by naming was good, but on asking the patient to place the finger of one hand upon a point stimulated on the opposite arm the results were poor. This is explained by the grave loss of the sense of passive position in the arms. Although the patient had the power of localizing the point stimulated, the arm failed to reach the point because of the loss of the sense of position and active movement.

During life there was no loss of painful or thermal sensibility. The posterior roots and their zone of entry into the posterior columns and posterior horns were only affected in a few segments by a very little recent degeneration. Therefore impulses underlying these forms of sensibility could pass directly into the posterior horn and then upward in the secondary sensory neurons, whose cell-stations lie in the posterior horn.

Tactile sensibility both to light touch and to pressure was unaffected. It is clear, therefore, that the posterior columns need not be intact for the upward passage of impulses concerned with tactile sensibility.

Though impulses concerned with touch and pressure may run up in the posterior columns for a short distance, yet there is always a second path for such impulses in the opposite half of the spinal cord along a secondary sensory path.

There was some evidence of a slight involvement of the pyramidal tracts during life. In the lower limbs there was slight stiffness on passive movement. Moreover, on several occasions a definite extensor response was obtained in the left great toe, but on other occasions no response, or a normal one, occurred. On the right side an extensor response was never obtained. These phenomena may be explained by the very slight lesions found in the pyramidal tracts.

The "tabetic type" of subacute combined degeneration has been clearly recognized, and of it this case forms a very well defined example.

P. Marie and Crouzon [5], in their "*Étude clinique de la forme tabétique des scléroses combinées*," consider that the form of combined sclerosis which simulates *tabes dorsalis* can be distinguished by three symptoms:—

- (1) A gait in which the legs are dragged along the ground.
- (2) Paraplegia.
- (3) Babinski's toe phenomenon.

In this case the gait was ataxic, but paraplegia was present; and at times a definite extensor response was obtained in the left great toe.

SUMMARY.

(1) The case is an example of "subacute combined degeneration," in which the lesions are almost confined to the long fibres of the posterior columns.

(2) The degeneration was associated with severe anæmia of a secondary type. The degeneration and anæmia were probably caused by toxins absorbed from a large, chronic, granulomatous ulcer in the stomach.

(3) The case shows that a complete lesion of the long fibres of the posterior columns of the spinal cord results in a loss of the sense of passive position, ataxia, and loss of discrimination of points and weights. Localization of touch is but little affected. This result agrees with the experiments of Page May [6], who has recently reviewed the experimental work upon this subject.

(4) Painful, thermal, and tactile impulses can ascend the cord, although the posterior columns are degenerated.

(5) The evidence derived from this case is at variance with the view of Pétren, that a lesion of the posterior column does not produce a loss of muscle-sense unless the dorsal spino-cerebellar tract in the same half of the spinal cord is likewise affected.

In conclusion, I must express my thanks to Dr. Hubert Turnbull for his assistance in the pathological part of this paper, and I am indebted to Dr. Farquhar Buzzard for much kind help in the interpretation of the Marchi preparations.

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PUBLICATIONS RECENTLY RECEIVED.

[Notes on a book under this heading do not preclude a subsequent review.]

Les Manifestations fonctionnelles des Psychonévroses, leur Traitement par la Psychothérapie. Par Professeur J. DEJERINE et Dr. E. GAUCKLER. Pp. 561. Paris: Masson, 1911.

For nearly thirty years Professor Dejerine has been interested in the treatment of the various psychoneuroses, and fifteen years ago he installed a ward in the Salpêtrière (Salle Pinel) definitely for isolation and psychotherapeutic treatment. For he had long been struck by the failure of the Weir Mitchell procedure, and of hypnotic and other forms of suggestion, when unaccompanied by re-education.

The first half of the book is devoted to a description of the varieties of functional disorders, and to the expression of the authors' views on hysteria, especially in relation to simulation and to emotional shock. In the second half the psychoneuroses are studied synthetically; auto-intoxication and exhaustion are rejected as true causal factors in the genesis of neurasthenia, and the importance of emotional shocks in evoking the condition is emphasized. Such a shock need not be an external occurrence, but may arise internally in the life of the patient; the secret sin, the unconfessed fault, disgusts, fears and other causes of emotion are considered in detail. Then follows an excellent chapter headed "Comment on devient neurasthénique."

The third part deals with treatment, especially psychotherapy. The introduction is a splendid indictment of the prevalent methods of treating psychical states, as if they could be cured by medication of the various organs of the body, and of the antitherapeutic suggestions so commonly implanted by the "Médecin organiciste." Dejerine holds that direct suggestion appeals to the automatism of the patient, and logically should be exerted during hypnosis. He points out the risks of reducing the patient to an automaton, and all its consequent dangers. Waking-suggestion he thinks less injurious, and acknowledges its success in the hands of certain physicians. His own method is that of persuasion. The patient is told the nature of his condition, and an attempt is made to awaken the different elements of his personality, and to force him to think and to understand. The methods of persuasion adopted by the author are explained in full, and another chapter is devoted to the accessories of the treatment, such as isolation.

Then follows a detailed description of the means used to combat the various phobias, based on functional visceral disturbances. Prophylaxis is explained, and this most instructive work closes with an appeal to all physicians to deliver their patients from visceral introspection, and to keep them free from harmful medical suggestion.

Die epidemische Kinderlähmung (Heine-Medinsche Krankheit). Von Professor Dr. PAUL. H. RÖMER. Mit 57 in dem Text gedruckten Abbildungen. S. 256. Berlin: Springer, 1911.

This is no mere compilation from the literature, but the record of an interesting and important series of observations, made during the Hesse-Nassau epidemic of 1909. Emulsions were made from the central nervous system of five children who had died with acute signs of poliomyelitis, and three proved to be infective to monkeys. These monkeys yielded three strains of infective material, which showed the characteristic reactions to cold, to heat, to glycerine, and to filtration. The incubation period, after injection into the central nervous system, with or without coincident injection into the peritoneum, was from three and a half to fifteen days. Rabbits were entirely immune. During the prodromal period the monkeys were lethargic, and frequently suffered from gastro-intestinal symptoms, and in three cases where the animals were sufficiently tame a considerable rise of temperature was shown to occur. The author believes that the door by which the virus enters the nervous system is the lymphatics from the mucous membrane of the throat or of the intestinal tract.

Sur l'Agnosie tactile. Par Dr. LÉON VOUTERS. Pp. 192. Paris: Steinheil, 1909.

The author of this Thesis reviews the statements of French, German, and English writers on the factors underlying tactile agnosia, and considers them in the light of his own observations at the Salpêtrière. He finds that want of tactile recognition is always associated with sensory defects, except in dementia and hysteria, and that motor loss alone is not sufficient to produce astereognosis. Tactile agnosia is of no value in localizing the site of the lesion, and there is no centre in the cortex devoted exclusively to recognition by touch of the significance of objects.

Archives of Neurology and Psychiatry from the Pathological Laboratory of the London County Asylums. Edited by FREDERICK WALKER MOTT, M.D., F.R.S. Vol. v, 1911. Pages not numbered consecutively after p. 226. London: King, 1911.

The first half of this volume contains papers by Dr. Mott and his fellow-workers which have not been published before, whilst the second half contains reprints of lectures "On the Cerebrospinal Fluid," "The Hereditary Aspects of Nervous and Mental Diseases" and of papers on "The Comparative Neuropathology of Trypanosome and Spirochaete Infections," and on the "Motor Localization in the Brain of the Gibbon correlated with a Histological Examination," besides some other smaller contributions. Amongst the many interesting contributions in this volume must be mentioned "Congenital Syphilis and Feeble-mindedness," a general statement on the whole question, by Dr. Mott; "The Psychological Conception of Insanity," by Dr. Bernard

Hart, and an excellent paper by Dr. Harper Smith on "Dementia Præcox." Dr. Gibson deals with the circulating changes in dementia præcox, and Dr. Pietro Rondoni reports the pathological examination of a case of tabo-paralysis with ophthalmoplegia.

La pratique neurologique. (Publiée sous la direction de Pierre Marie.)

Par MM. O. CROUZON, G. DELAMARE, E. DESNOS, GEORGES GUILLAIN, E. HUET, LANNOIS, A. LÉRI, F. MOUTIER, POULARD, ROUSSY. *Secrétaire de la Rédaction*: O. Crouzon. Avec 302 figures dans le texte. Pp. 1402. Paris: Masson, 1911.

Marie introduces this volume, which has been written and edited by his old pupils, as one specially intended for students and general practitioners. He claims that while its chief aim is the interpretation of the symptoms of nervous disorders it is not merely what the French call a *Sémiologie*, a treatise on symptoms, but that it deals in addition with all the means of arriving at an anatomical as well as a clinical diagnosis.

Yet it is in this very particular that the volume fails most seriously. But few diseases are dealt with as such; most of the chapters are devoted to the consideration of certain symptoms, as sensory disturbances, muscular atrophies, inco-ordination, &c., and an enumeration of the various conditions in which they may occur. In many cases the most usual associations of symptoms which characterize definite diseases are given, but rarely so fully as to provide a clear picture of the disorder. Syringomyelia for instance is referred to in the sections on the disturbances of sensibility, muscular atrophy, trophic disturbances and skeletal deformities, but there is nowhere such a collected description of its symptomatology as would enable a student who had studied the volume to recognize a case of the disease. Similarly acromegaly is only referred to incidentally in different chapters, while amyotrophic lateral sclerosis is dismissed in a few lines.

Even as a treatise on symptoms and their significance the volume is not wholly satisfactory. This is chiefly due to the fact that pathology is almost completely neglected; not only is there little or no reference to the anatomical changes to which any symptom or disorder may be due, but even the nature and origin of defined anatomical processes is rarely referred to. The student who relies on *La pratique neurologique* will consequently find difficult that correlation of clinical symptoms and structural changes on which the accurate diagnosis of organic diseases of the nervous system depends.

On the other hand, in a volume of this size devoted mainly to the interpretation of clinical symptoms a fuller and more critical analysis of the significance of each symptom might be expected than is generally to be found. And by a little pruning of some of the more diffuse articles space could have been obtained for a valuable bibliography relating to each section.

Many of the sections are extremely interesting and well written, as those

on sensation by Roussy, on tremors by Crouzon, on the ocular symptoms of nervous origin by Poulard, and on the deformities and palsies of the hand and foot by Léri; but, as must be expected where so many collaborators are engaged, in such a work there is considerable unevenness and a disproportion between the different chapters.

One of the most interesting features of the volume is the amount of space that has been allotted to the sections on treatment, but unfortunately owing to the form which it has taken the text generally suggests the treatment of symptoms rather than of the diseases themselves.

Conduct and its Disorders Biologically Considered. By CHARLES ARTHUR MERCIER, M.D., F.R.C.P. Pp. 377. London: Macmillan, 1911.

Conduct, as it appears in ethics or history, has always occupied the human mind, but no one has attempted to deal with conduct as a whole scientifically. Dr. Mercier has set himself this gigantic task, and has produced a book written with all that lucidity and clear enunciation of his views for which he is justly distinguished. The biological principle which governs his attitude towards the problem of conduct is estimation of its value in securing the survival of man in the struggle for existence.

The first book is devoted to a consideration of action, the second to conduct, and the most complex as well as the simplest acts are measured against this standard of utility. Conduct is considered as self-conservative, in relation to the community and in connexion with the race. All acts, whether of the individual or community, are treated as if they were logical and directed to one end; nothing is fortuitous or irrational. This attitude towards the facts is most evident in the chapters on Fashion, Courtship and *Æsthetics*. As might be expected, the chapter on Religion is the weakest in the book.

Elements of Physiological Psychology. By G. T. LADD, LL.D., and R. S. WOODWORTH, Ph.D. Pp. 704. New York: C. Scribner's Sons, 1911.

This text-book, which appeared first in 1887, has been entirely re-written, and is in reality a new work. It is excellently arranged for the student, and for reference. The first part deals with the nervous mechanism and forms an up-to-date physiology of the nervous system. In the second part a systematic attempt is made to correlate mental phenomena, such as sensations, with the activities of the nervous mechanism, whilst the third part deals with the nature of mind. It is concisely written and contains references to all the recent advances in experimental psychology.

Leitfaden der physiologischen Psychologie. In 15 Vorlesungen. Von Professor Dr. TH. ZIEHEN. Neunte teilweise umgearbeitete Auflage mit 32 Abbildungen im Text. S. 314. Jena: Fischer, 1911.

The ninth edition of this well-known text-book contains no fundamental changes from the eighth, which was fully noticed in this Journal on its appearance. The copious references to works not usually consulted by neurologists add greatly to its value.

Outlines of Psychiatry. By WILLIAM A. WHITE, M.D. Third Edition revised and enlarged. Pp. 272. New York: Journal of Nervous and Mental Disease Publishing Company, 1911.

This forms one of a series of monographs on nervous and mental disease intended for the practitioner and senior student. An unusually full scheme is given for examining the patient which can be modified to suit each case. The following chapters are short descriptive accounts of maniacal-depressive insanity, dementia paralytica, dementia præcox, involution melancholia and the senile psychoses. These are the best in the book, which at the end tends to become a catalogue of insane conditions arranged according to the disease with which they are associated. The popularity of this work is shown by the fact that it has already reached a Third Edition.

Meningitis, Sinus Thrombosis and Abscess of the Brain. By JOHN WYLLIE, M.D. Pp. 258. London: Lewis, 1911.

This book appears to be a compilation from the opinions of others by one who has had little personal experience of the conditions he describes. He speaks of finding the *Spirochæta pallida* in the blood in cases of syphilitic meningitis, and evidently is not familiar with the significance of the recent work on the Wassermann reactions in cerebrospinal fluid. Lumbar puncture is described in full, but the needle is to be "passed 1.5 to 3 cm. into the third or fourth lumbar interspace." None of the well-known difficulties in diagnosis in cerebral abscess and none of the recent methods of examination are mentioned.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-81, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I. to XXIII. inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

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TO

BRAIN:

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FOR

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